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# TRANSACTIONS

OF THE

# COLLEGE OF PHYSICIANS

OF

# PHILADELPHIA

THIRD SERIES

VOLUME THE FORTY-SEVENTH

PHILADELPHIA
PRINTED FOR THE COLLEGE
1925

# NOTICE

The present volume of TRANSACTIONS contains the papers read before the College from January, 1925, to December, 1925, inclusive.

The Committee of Publication thinks it proper to say that the College holds itself in no way responsible for the statements, reasonings, or opinions set forth in the various papers published in its TRANSACTIONS.

EDITED BY

WALTER G. ELMER, M.D.

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DORNAN, PRINTER

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OF THE

# PRESIDENTS OF THE COLLEGE FROM THE TIME OF ITS INSTITUTION

| ELECTED | |
|---|---|
| 1787 | JOHN REDMAN |
| 1805 | WILLIAM SHIPPEN |
| 1809 | ADAM KUHN |
| 1818 | THOMAS PARKE |
| 1835 | THOMAS C. JAMES[1] |
| 1835 | THOMAS T. HEWSON |
| 1848 | GEORGE B. WOOD |
| 1879 | W. S. W. RUSCHENBERGER |
| 1883 | ALFRED STILLÉ |
| 1884 | SAMUEL LEWIS[2] |
| 1884 | J. M. DA COSTA |
| 1886 | S. WEIR MITCHELL |
| 1889 | D. HAYES AGNEW |
| 1892 | S. WEIR MITCHELL |
| 1895 | J. M. DA COSTA |
| 1898 | JOHN ASHHURST, JR. |
| 1900 | W. W. KEEN |
| 1902 | HORATIO C. WOOD |
| 1904 | ARTHUR V. MEIGS |
| 1907 | JAMES TYSON |
| 1910 | GEORGE E. DE SCHWEINITZ |
| 1913 | JAMES CORNELIUS WILSON |
| 1916 | RICHARD H. HARTE |
| 1919 | WILLIAM J. TAYLOR |
| 1922 | THOMAS R. NEILSON |
| 1925 | HOBART A. HARE |

[1] Died four months after his election.
[2] Resigned on account of ill-health.

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1925

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# FELLOWS

OF THE

# COLLEGE OF PHYSICIANS OF PHILADELPHIA

## DECEMBER, 1925

* Non-resident Fellows. † Fellows who have commuted dues. ‡ Deceased.

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ELECTED

1892. Abbott, Alexander Crever, M.D., Sc.D., Dr. P.H., Professor of Hygiene and Bacteriology and Director of the School of Hygiene and Public Health, University of Pennsylvania. 4016 Pine St.

1921. Addison, William H. F., A.B., M.D., Professor of Normal Histology and Embryology in the University of Pennsylvania. Medical Laboratories, University of Pennsylvania.

1905. Adler, Lewis H., Jr., M.D., Formerly Professor of Proctology in the Graduate School of Medicine, University of Pennsylvania; formerly Prosector to the Professor of Anatomy in the University of Pennsylvania; Consulting Surgeon to the Charity Hospital. 313 S. Seventeenth St.

1914. Aiken, Thomas Gerald, M.D., Physician-in-Chief to the Chester County Hospital, West Chester, Pa.; Pathologist to the Country Branch of the Rush Hospital for Tuberculosis. Berwyn, Pa.

1913. Alexander, Emory G., M.D., Surgeon to St. Christopher's Hospital for Children; Associate Surgeon to the Episcopal Hospital; Clinical Professor of Surgery in the Woman's Medical College of Pennsylvania; Demonstrator of Fracture Dressings in the Jefferson Medical College, and Assistant Surgeon to the Kensington Hospital for Women. 337 S. Eighteenth St.

ELECTED

1906. Allen, Francis Olcott, Jr., A.B., M.D., Surgeon to the Presbyterian Hospital; Associate Surgeon to the Pennsylvania Hospital. 2216 Walnut St.

1896. Allyn, Herman B., A.B., M.D., Physician to the Philadelphia General Hospital. 3910 Chestnut St.

1888. Anders, James M., M.D., LL.D., Professor of Medicine and Clinical Medicine in the Medico-Chirurgical College; Officer de l'Instruction Publique. 250 S. Seventeenth St.

1905. Anspach, Brooke M., M.D., Professor of Gynecology in the Jefferson Medical College; Attending Gynecologist, Jefferson Hospital; Gynecologist to the Stetson Hospital; Attending Gynecologist to the Bryn Mawr Hospital. 1827 Spruce St.

1905. Appleman, Leighton F., M.D., Attending Surgeon to the Wills Eye Hospital; Associate Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Ophthalmologist to the Frederick Douglass Memorial Hospital and to the Burd School; Demonstrator of Pharmacy and Materia Medica, and Instructor in Therapeutics in the Jefferson Medical College. 308 S. Sixteenth St.

1922. Arnett, John Hancock, A.B., M.D., Instructor in Medicine, Medical School, University of Pennsylvania; Assistant in Medicine and Students' Physician, University Hospital. 262 S. Twenty-first St.

1906. Ashhurst, Astley Paston Cooper, A.B., M.D., Professor of Clinical Surgery, University of Pennsylvania; Surgeon to the Episcopal Hospital and to the Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases. 257 S. Sixteenth St.

1893. Ashton, Thomas G., M.D., Physician to the Philadelphia General Hospital. Wynnewood, Pa.

1920. Astley, George Mason, M.D., Assistant Surgeon, Samaritan Hospital. 5317 Master St.

1914. Austin, J. Harold, B.S. (Univ. of Penna.), M.D., Professor of Research Medicine, University of Pennsylvania. John Herr Musser Department of Research Medicine, University of Pennsylvania.

1906. Babbitt, James A., A.B. (Yale), A.M. (Haverford), M.D., Assistant Professor of Otology, University of Pennsylvania; Associate Professor of Oto-Laryngology, Graduate School of Medicine, University of Pennsylvania; Assistant Laryn-

ELECTED

gologist and Aurist, Lankenau Hospital; Laryngologist, Mary Drexel Children's Hospital. 1912 Spruce St.

1910. Baer, Benjamin F., Jr., B.S., M.D., Associate Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Assistant Ophthalmologist, University Hospital; Consultant Ophthalmologist, Philadelphia Lying-in Charity Hospital. 1927 Spruce St.

†1892. Baker, George Fales, B.S., M.D. 1818 Spruce St.

1911. Baldwin, James Harvey, A.B., M.D., Surgeon to the Methodist Hospital. 1426 Pine St.

1889. Baldy, John Montgomery, M.D., Surgeon to the Gynecean Hospital; Consulting Surgeon to the Jewish and the Frederick Douglass Memorial Hospitals. Devon, Pa.

1916. Balentine, Percival L., M.D., Assistant Surgeon, Wills Eye Hospital; Demonstrator of Ophthalmic Surgery in the Philadelphia Polyclinic. 302 Weightman Building, 1524 Chestnut St.

1898. Balliet, Tilghman M., A.M., M.D., Professor of Therapeutics at Dartmouth College, Hanover, N. H.; Physician to the Old Man's Home. 3920 Sansom St.

1911. Barnard, Everett P., M.D., Obstetrician to the Maternity Hospital; Assistant Instructor in Obstetrics in the University of Pennsylvania. 245 S. Eighteenth St.

1924. Bartle, Henry J., B.S., M.D., Clinical Assistant, Out-patient Medical Department, Lankenau Hospital; Clinical Assistant, Department for Diseases of the Stomach and Bowels, Jefferson Medical College and Hospital. 2018 Chestnut St.

1921. Bauer, Edward L., M.D., Consultant Pediatrist, Germantown Hospital; Visiting Physician, Philadelphia Hospital for Contagious Diseases; Assistant Visiting Physician, Children's Hospital of the Mary J. Drexel Home. 6112 Germantown Ave.

1883. Baum, Charles, A.M., M.D., Ph.D. 1828 Wallace St.

1922. Bazett, Henry Cuthbert, M.A., M.D. (Oxon.), F.R.C.S. (England), Professor of Physiology, University of Pennsylvania. Bryn Mawr, Pa.

1908. Beardsley, Edward J. G., M.D., L.R.C.P. (Lond.), Associate Professor of Medicine in the Jefferson Medical College; Chief Clinical Assistant in the Out-patient Medical Department of the Jefferson Medical College Hospital; Assistant Physician to the Jefferson Hospital. 1919 Spruce St.

ELECTED

*1916. Bell, William Hemphill, M.D., Captain, Medical Corps, U. S. Navy, Senior Medical Officer and Head of Department of Hygiene, U. S. Naval Academy, Annapolis, Maryland.

1923. Bergey, David H., A.M., M.D., B.S., Dr. P.H., Assistant Professor of Hygiene and Bacteriology, University of Pennsylvania. 206 S. Fifty-third St.

*1903. Biggs, Montgomery H., M.D., Surgeon to the Rutherford Hospital; Chief Surgeon of the Carolina, Churchfield and Ohio Railway. Rutherfordton, N. C.

1918. Billings, Arthur E., M.D., Clinical Assistant in Surgery, Dept. B, Jefferson Medical College; Surgeon to Pennsylvania and Bryn Mawr Hospitals. 2020 Spruce St.

1917. Birdsall, Joseph C., A.B., A.M., M.D., Urologist, Polyclinic Section of the Medico-Chirurgical College and Hospital, Graduate School of Medicine, University of Pennsylvania; Assistant in Genito-urinary Dispensary, Presbyterian Hospital; Instructor in Surgery, University of Pennsylvania. 4610 Spruce St.

1908. Bland, Pascal Brooke, M.D., Professor of Obstetrics, Jefferson Medical College; Visiting Obstetrician, Jefferson Medical College; Gynecologist to St. Joseph's Hospital. 1621 Spruce St.

1917. Block, Frank B., A.B., M.D., Surgeon to the Jewish Hospital; Instructor in Gynecology in the University of Pennsylvania. Medical Arts Building.

1894. Bochroch, Max H., M.D., Neurologist to the St. Joseph's and Jewish Hospitals; Physician to the Psychopathic Wards of the Philadelphia General Hospital. 1539 Pine St.

1896. Boger, John A., A.M., M.D., Surgeon to St. Mary's Hospital; Surgeon to the Stetson Hospital; Surgeon to the Dispensary of the Episcopal Hospital. 2213 N. Broad St.

1923. Bond, Earl D., A.B., M.D., Physician-in-Chief, Pennsylvania Hospital, Department for Mental and Nervous Diseases; Professor of Psychiatry, Graduate School of Medicine, Univeristy of Pennsylvania. Bryn Mawr, Pa.

1911. Bonney, Charles W., A.B., M.D., Associate in Topographic and Applied Anatomy in the Jefferson Medical College. 1117 Spruce St.

1924. Boon, David J., M.D., Opthalmologist, Memorial Hospital and Philadelphia Hospital for Contagious Diseases; Assistant Ophthalmic Surgeon, Episcopal Hospital. 1532 N. Fifteenth Street.

ELECTED

1921. Borzell, Francis Frank, M.D., Roentgenologist, Frankford Hospital; Chief Clinical Assistant, Roentgen Department, Jefferson Medical College; *X*-Ray Consultant, State Hospital for the Insane, Norristown, Pa. 4910 Frankford Ave.

1913. Boston, L. Napoleon, A.M., M.D., Professor of Physical Diagnosis in the Medico-Chirurgical College; Physician to the Philadelphia General Hospital; Pathologist to the Frankford Hospital. 2024 Chestnut St.

1919. Bowen, David Ralph, M.D., Radiologist to the Pennsylvania Hospital. 82 W. Lacrosse Ave., Lansdowne, Pa.

1923. Bower, John O., M.D. 2008 Walnut St.

1891. Boyd, George M., M.D., Professor of Obstetrics, Graduate School of Medicine, University of Pennsylvania; Consultant to the Philadelphia Lying-in Charity; Consulting Obstetrician to the Preston Retreat; Obstetrician and Gynecologist to the Medico-Chirurgical Hospital. 1909 Spruce St.

1907. Boyer, Henry Percival, M.D., Neurologist to the Stetson Hospital; Physician to the Philadelphia Home for Incurables; Assistant Physican to the Orthopædic Hospital and Infirmary for Nervous Diseases. 4602 Baltimore Ave.

1925. Boykin, Irvine M., M.D., Associate Surgeon to Episcopal Hospital; Instructor in Surgery, Graduate School of Medicine, University of Pennsylvania. Elkins Park, Pa.

1907. Bradley, William N., Ph.G., M.D., Visiting Pediatrist to Howard Hospital; Visiting Pediatrist to Philadelphia General Hospital; Associate in Pediatrics, School of Medicine, University of Pennsylvania; Associate in Pediatrics, Graduate School of Medicine, University of Pennsylvania. 1725 Pine St.

1923. Braisted, William C., M.D., Ph.B., LL.D., D.Sc., F.R.C.S. (Edin.), Surgeon-General, U. S. Navy, retired; President, Philadelphia College of Pharmacy and Science. West Chester, Pa.

1921. Bransfield, John W., M.D., Clinical Professor of Surgery, Woman's Medical College; Visiting Surgeon to St. Agnes, St. Vincent's and Woman's College Hospitals. 2025 Walnut Street.

1903. Branson, Thomas F., M.D., Attending Physician to the Bryn Mawr Hospital. Rosemont, Pa.

1891. Brinton, Lewis, M.D., Physician-in-Chief to the American Hospital for Diseases of the Stomach. 1301 Medical Arts Bldg., Sixteenth and Walnut Sts.

ELECTED

1900. Brinton, Ward, A.M., M.D., Clinical Professor of Medicine, Woman's Medical College of Pennsylvania; Instructor in Medicine, University of Pennsylvania; Chief of Division of Tuberculosis, Department of Public Health of Philadelphia; Visiting Physician, Department for Tuberculosis, Philadelphia General Hospital. 1423 Spruce St.

1917. Bromer, Ralph S., A.B. (Yale), M.D., Roentgenologist to the Episcopal and the Orthopædic Hospitals. 504 W. Mt. Airy Ave.

1919. Brown, H. MacVeagh, M.D., Associate Physician, Presbyterian Hospital. 4608 Baltimore Ave.

1919. Brown, Henry P., Jr., M.D., Surgeon to Pennsylvania and Children's Hospitals; Assistant Surgeon, Presbyterian Hospital. 2134 Spruce St.

1916. Brown, Samuel Horton, M.D. 1901 Mt. Vernon St.

1887. Brubaker, Albert P., A.M., M.D., Professor of Physiology and Medical Jurisprudence in the Jefferson Medical College. 3426 Powelton Ave.

1916. Buckley, Albert Coulson, M.D., Medical Superintendent, Friends' Hospital, Frankford; Associate Professor of Psychiatry, Graduate School of Medicine, University of Pennsylvania. Frankford, Phila.

1906. Burns, Stillwell C., M.D., Associate Professor of Surgery in the Graduate School of Medicine, University of Pennsylvania. 1925 Spring Garden St.

1892. Burr, Charles W., M.D., Professor of Mental Diseases in the University of Pennsylvania; Neurologist to the Philadelphia General Hospital. 1918 Spruce St.

1906. Butler, Ralph, M.D., Professor of Diseases of the Nose and Throat in the Philadelphia Polyclinic and the College for Graduates in Medicine; Chief of the Dispensary for Diseases of the Ear at the University Hospital; Assistant Professor of Otology in the University of Pennsylvania; Laryngologist and Aurist to the Lankenau Hospital. 2007 Chestnut St.

*1908. Cadbury, William W., A.M., M.D., Canton Christian College, Canton, China.

†1907. Cadwalader, Williams B., M.D., Assistant Professor of Neurology, School of Medicine, University of Pennsylvania; Neurologist to the Presbyterian Hospital; Consulting Neurologist to the Bryn Mawr Hospital. 1206 Medical Arts Building.

ELECTED

1905. Carmany, Harry S., M.D., Surgeon to Memorial Hospital, Roxborough; Associate Surgeon of the Episcopal Hospital; Surgeon to the Dispensary of the Episcopal Hospital. 366 Green Lane, Roxborough.

1924. Carncross, Horace, M.D., 1003 Spruce St.

1910. Carnett, John Berton, M.D., Professor of Surgery, Graduate School of Medicine, University of Pennsylvania; Associate in Surgery, Medical Department, University of Pennsylvania; Surgeon to Philadelphia General Hospital; Chief Surgeon to the American Stomach Hospital. 2012 Spruce St.

1905. Carpenter, Herbert B., M.D. 1805 Spruce St.

1895. Carpenter, John T., M.D., Attending Ophthalmologist to the Bryn Mawr Hospital. 2030 Chestnut St.

1917. Carson, John B., M.D., Physician to Episcopal Hospital; Assistant Physician, Pennsylvania Hospital. 1802 Pine Street.

1922. Case, Eugene A., M.D., Associate Professor of Pathology, University of Pennsylvania; Assistant Pathologist, Philadelphia General Hospital. Lansdowne, Pa.

1900. Chance, Burton, M.D., Attending Surgeon to the Wills Eye Hospital; Consulting Ophthalmologist Eastern Pennsylvania Institution for the Feeble-minded and Epileptics; Ophthalmic Surgeon to the Pennsylvania Railroad Company. 315 S. Fifteenth St.

1897. Cheston, Radcliffe, M.D., Visiting Physician to the Chestnut Hill Hospital; Consulting Physician to the Germantown Hospital and to the Pennsylvania Institution for the Deaf and Dumb. Chestnut Hill.

1903. Chrystie, Walter, M.D. One of the Senior Physicians to Bryn Mawr Hospital. Bryn Mawr, Pa.

1899. Clark, John G., M.D., Professor of Gynecology in the University of Pennsylvania; Gynecologist-in-Chief to the University Hospital. 2017 Walnut St.

1910. Cloud, J. Howard, M.D., Attending Physician to the Bryn Mawr Hospital. 11 W. Montgomery Ave., Ardmore, Pa.

1903. Coates, George Morrison, A.B., M.D., Professor of Otology, Graduate School of Medicine, University of Pennsylvania; Associate Surgeon, Ear, Throat and Nose, Pennsylvania Hospital; Consulting Laryngologist to the Philadelphia Orphanage and to the Sharon Hospital, Sharon, Conn. 1721 Pine St.

ELECTED

1908. Codman, Charles A. E., M.D., Physician to the American Oncologic Hospital. 4116 Spruce St.

1922. Cohen, Leon Solis, A.B., M.D., Clinical Assistant of Roentgenology, Jefferson Medical College. 1923 Spruce St.

1907. Cohen, Myer Solis, A.B., M.D., Assistant Professor in Medicine, Graduate School of Medicine, University of Pennsylvania; Lecturer on Medical Jurisprudence, Woman's Medical College of Pennsylvania; Director of the Jules E. Mastbaum Research Laboratory of the Jewish Hospital; Pediatrist to the Jewish Hospital. 1833 Pine St.

1888. Cohen, Solomon Solis, M.D., Professor of Clinical Medicine in the Jefferson Medical College; Physician to the Jefferson Medical College Hospital, to the Philadelphia General Hospital, to the Jewish Hospital and to the Rush Hospital. 1906 Walnut St.

1920. Cole, Charles J., A.B., M.D., Visiting Physician, Philadelphia Hospital for Contagious Diseases; Assistant Pediatrist, Polyclinic Hospital; Physician to Out-patient Department, Mary Drexel Home; Assistant Physician to Out-patient Department, Children's Hospital, University Hospital. Elkins Park, Pa.

1898. Coles, Stricker, M.D. Bryn Mawr, Pa.

*1901. Coley, Thomas Luther, A.B., M.D., Major, Medical Corps, U. S. Army. Fortress Monroe, Va.

1903. Coplin, W. M. L., M.D., Professor of Pathology in the Jefferson Medical College; Pathologist to and Director of the Laboratories of the Jefferson Medical College Hospital; Pathologist to the Philadelphia General Hospital and to the Friends' Asylum for the Insane, Frankford; Bacteriologist to the Pennsylvania State Board of Health. Albany Apartments, Atlantic City, N. J.

1912. Copp, Owen, A.B., M.D., Consultant for the Future Development of the Pennsylvania Hospital. 4401 Market St.

1911. Cornell, Walter Stewart, A.B., M.D., Director of Medical Inspection of Public Schools of the City of Philadelphia; Chief of Medical Staff of the House of Detention; Lecturer on Osteology in the University of Pennsylvania. 1919 Cherry St.

1914. Corson, Edward Foulke, M.D., Assistant Professor of Dermatology, Jefferson Medical College; Dermatologist, Children's Hospital of Philadelphia. 1927 Spruce St.

ELECTED

1907. Council, Malcolm S., M.D., Attending Physician to the Bryn Mawr Hospital; Attending Physician to the Cathcart Home at Devon. Bryn Mawr, Pa.

1924. Cowan, Alfred, M.D., Associate in Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Assistant Surgeon, Wills Hospital; Assistant Dispensary Surgeon, University Hospital; Assistant Instructor in Ophthalmology, School of Medicine, University of Pennsylvania. 2007 Pine Street.

1904. Craig, Frank A., M.D., Instructor in Medicine in the University of Pennsylvania; Visiting Physician to the Henry Phipps Institute, University of Pennsylvania; Visiting Physician to the White Haven Sanatorium; Tuberculosis Consultant to the Presbyterian Hospital. 2011 Pine Street.

1907. Crampton, George S., M.D., Attending Surgeon to the Eye Department of the Pennsylvania Hospital and the Philadelphia Hospital for Contagious Diseases; Assistant Surgeon to the Wills Hospital; Lecturer on Physiologic Optics in the Philadelphia Polyclinic and School for Graduates in Medicine; Ophthalmologist to the Philadelphia Orphanage. 1819 Walnut St.

1924. Crawford, Baxter Lindsey, M.D., Associate in Pathology, Jefferson Medical College; Chief of Laboratory Service, Jefferson Hospital; Assistant Pathologist, Philadelphia General Hospital. Jefferson Hospital, Tenth and Sansom Sts.

1920. Creighton, William J., B.A., M.D., Assistant Ophthalmic Surgeon, Germantown Hospital and Dispensary; Assistant Dispensary Surgeon, Department Ophthalmology, University Hospital; Instructor in Ophthalmology, University of Pennsylvania Medical School. 1905 Chestnut St.

1920. Cross, George Howard, M.D., Ophthalmologist to the Chester Hospital; Instructor in Ophthalmology, Graduate School of Medicine, University of Pennsylvania. Chester, Pa.

1917. Cross, Sumner H., A.B., M.D., Physician to the Abington Memorial Hospital, Abington, Pa. 412 York Road, Jenkintown, Pa.

1921. Crossan, Edward T., M.D., N. E. Cor. Sixteenth and Spruce Streets.

1924. Crowell, Bowman C., A.B., M.D., C.M., Professor of Pathology, Jefferson Medical College; Pathologist, Jefferson Hospital; Attending Pathologist, Philadelphia General Hospital. "The Gladstone."

ELECTED

1904. Cruice, John M., M.D., Physician to the Henry Phipps Institute of the University of Pennsylvania; Physician to the Medical Dispensary of St. Agnes' Hospital; Instructor in Medicine in the University of Pennsylvania. 2021 Pine Street.

*1910. Cummins, W. Taylor, M.D., Pathologist to the Southern Pacific Hospital; Director of the Mary W. Harriman Research Laboratory, San Francisco, Calif.

1902. Currie, Charles A., M.D., Physician to the Germantown Hospital. West Walnut Lane, Germantown.

1896. Da Costa, John Chalmers, M.D., Professor of the Principles of Surgery and of Clinical Surgery in the Jefferson Medical College; Surgeon to the Philadelphia General and St. Joseph's Hospitals. 2045 Walnut St.

1887. Daland, Judson, M.D., Professor of Medicine, Graduate School of Medicine, University of Pennsylvania. 317 S. Eighteenth St.

1919. Davies, John R., Jr., M.D., Chief to the Out-patient Nose, Throat and Ear Department of the Pennsylvania, Bryn Mawr and Chestnut Hill Hospitals. 302 S. Nineteenth Street.

1896. Davis, Charles N., M.D., Dermatologist to the Pennsylvania Hospital; Consulting Dermatologist to St. Agnes' Hospital; Assistant Physician to the Dispensary for Skin Diseases in the Howard Hospital. 1931 Spruce St.

1916. Davis, Warren B., M.D., Rhinologist, Laryngologist, and Otologist, St. Agnes' Hospital; Instructor in Surgery, Jefferson Medical College; Assistant Surgeon, Frankford Hospital. 135 S. Eighteenth St.

1900. Davisson, Alex. Heron, M.D. 4514 Springfield Ave.

1894. Deaver, Harry C., M.D., Professor of Surgery in the Woman's Medical College of Pennsylvania; Surgeon to the Episcopal Hospital and to the Children's Hospital of the Mary J. Drexel Home; Surgeon-in-Chief to the Kensington Hospital for Women. 337 S. Eighteenth St.

1887. Deaver, John B., M.D., D.Sc., LL.D., John Rea Barton Professor of Surgery, University of Pennsylvania; Visiting Surgeon, Hospital of the University of Pennsylvania; Surgeon-in-Chief to the Lankenau Hospital. 1634 Walnut Street.

1902. Dehoney, Howard, M.D. 240 S. Thirteenth St.

ELECTED

1924. Deichler, L. Waller, M.D., Assistant Surgeon, Wills Hospital; Instructor Ophthalmology, University of Pennsylvania; Ophthalmologist, Philadelphia General Hospital. 1737 Chestnut St.

1923. De Long, Perce, M.D. 1909 Chestnut St.

1885. Dercum, Francis X., A.M., M.D., Ph.D., Professor of Nervous and Mental Diseases in the Jefferson Medical College; Consulting Neurologist to the Philadelphia General Hospital; Foreign Corresponding Member of the Neurological Society of Paris, and Corresponding Member of the Psychiatric and Neurological Society of Vienna. 1719 Walnut St.

1912. Dewey, J. Hiland, Ph.B., M.D., Assistant Surgeon to Wills Hospital; Ophthalmic Surgeon to St. Francis' Hospital, Trenton, N. J. 1436 Diamond St.

*1911. Dickson, Frank D., M.D. 1807 Federal Reserve Bank Building, Kansas City, Mo.

1908. Dillard, Henry K., Jr., M.D., Physician to the Out-patient Department of the Pennsylvania Hospital; Physician to the Dispensary of the Mary J. Drexel Home. 234 S. Twentieth St.

1924. Dillon, Edward S., A.B., M.D., Assistant Physician, Pennsylvania Hospital; Assistant Instructor in Medicine, School of Medicine, University of Pennsylvania. 2040 Pine St.

1920. Diven, John, A.B., M.D., Pediatrician to St. Christopher's Hospital and Babies' Hospital of Philadelphia. 2002 Spruce Street.

1920. Doane, Joseph Chapman, M.D., Superintendent and Medical Director, Philadelphia General Hospital; Associate Professor of Internal Medicine, Graduate School of Medicine, University of Pennsylvania. Philadelphia General Hospital.

*1897. Dorland, W. A. Newman, A.M., M.D., Professor of Gynecology in the Post-graduate Medical School of Chicago; Professor of Obstetrics in the Chicago College of Medicine and Surgery; Visiting Obstetrician to Cook County Hospital. 25 East Washington Street, Chicago, Ill.

1907. Dorrance, George Morris, M.D., Professor of Maxillo-Facial Surgery, Thomas Evans Institute, University of Pennsylvania; Professor of Surgery and Clinical Surgery, Woman's Medical College; Surgeon in Chief, Woman's College Hospital; Surgeon to St. Agnes' Hospital. 2025 Walnut St.

1902. Downs, Robert N., Jr., M.D., Surgeon to the Dispensary of the Germantown Hospital. 6008 Greene St., Germantown.

ELECTED

1910. Drayton, William, Jr., M.D., Physician to the Philadelphia Hospital for Contagious Diseases; Physician to the Out-patient Department of the Pennsylvania Hospital; Physician to the Pennsylvania Institute for the Instruction of the Blind; Assistant Physician to the Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases. 1820 Pine Street.

1911. Earnshaw, Henry Culp, M.S., M.D., Attending Physician to the Hospital of the Good Shepherd, Rosemont; Assistant Attending Physician to the Bryn Mawr Hospital; Attending Physician to the Bryn Mawr Children's Hospital; Pennsylvania Railroad Surgeon. Bryn Mawr, Pa.

*1887. Edwards, William A., M.D., Professor of Pediatrics in the Medical Department of the University of California. R. D. 2, Box 105, El Cajon, Calif.

1924. Egbert, Seneca, M.D., Professor of Hygiene, University of Pennsylvania. Wayne, Pa.

1911. Eliason, Eldridge E., B.A., M.D., Sc.D., Associate in Surgery in the University of Pennsylvania; Surgeon to the Howard Hospital; Assistant Surgeon to the University of Pennsylvania Hospital, the Philadelphia General Hospital and the American Stomach Hospital. 330 S. Sixteenth St.

1904. Elmer, Walter G., B.S., M.D., Associate Professor of Orthopædic Surgery, Graduate School of Medicine, University of Pennslvania; Clinical Professor of Orthopædic Surgery in the Woman's Medical College of Pennsylvania; Orthopædic Surgeon to the Polyclinic Hospital and to the Philadelphia General Hospital. 1801 Pine St.

1896. Ely, Thomas C., A.M., M.D. 3912 Chestnut St.

1893. Eshner, Augustus A., M.D., Consulting Physician to Mercy Hospital. 1019 Spruce St.

*1905. Evans, Joseph S., Jr., A.B., M.D., Professor of Medicine, Medical School, University of Wisconsin; Physician to State of Wisconsin General Hospital; Consulting Physician, Madison General and St. Mary's Hospitals. 1300 University Ave., Madison, Wis.

1905. Evans, William, M.D. 4007 Chestnut St.

1912. Eves, Curtis C., M.D., Otolaryngologist to Out-patient Department of the Pennsylvania Hospital; Attending Otolaryngologist to Bryn Mawr Hospital. 247 S. Seventeenth Street.

ELECTED

1894. Faries, Randolph, M.D. 2030 Chestnut St.

1922. Farley, David L., B.S., M.D., Instructor in Medicine, University of Pennsylvania; Assistant Physician, Pennsylvania Hospital. 1906 Pine St.

†1903. Farr, Clifford B., A.M., M.D., Director of Laboratories, Pennsylvania Hospital, Department for Mental and Nervous Diseases. Bryn Mawr, Pa.

1893. Farr, William W., M.D., Physician to the Leamy Home. 121 Maplewood Ave., Germantown.

1884. Fenton, Thomas H., M.D., Ophthalmic Surgeon to St. Vincent's Home, the Baptist Home and the Widener Home for Crippled Children. 1319 Spruce St.

1907. Fetterolf, George, A.B., M.D., Sc.D., Professor of Otolaryngology, University of Pennsylvania. 2010 Spruce St.

1924. Fewell, Alexander G., M.D. 1924 Pine St.

1907. Fife, Charles A., A.B., M.D., Associate in Pediatrics in the University of Pennsylvania; Pediatrist to the Presbyterian Hospital; Physician to the St. Christopher's Hospital for Children; Assistant Physician to the Philadelphia General Hospital. 2104 Spruce St.

1884. Fisher, Henry M., M.D. Jenkintown, Pa.

1910. Fisher, John Monroe, M.D., Associate Professor of Gynecology in the Jefferson Medical College; Gynecologist to the Philadelphia, St. Agnes' and Pottstown Hospitals; Assistant Gynecologist to the Jefferson Medical College Hospital. 345 S. Nineteenth St.

1888. Flick, Lawrence F., M.D. 736 Pine St.

1916. Forst, John R., M.D. 166 W. Coulter St., Germantown.

1908. Foulkrod, Collin, M.D., Obstetrician to the Presbyterian Hospital; Assistant Demonstrator of Obstetrics in Jefferson Medical College. 3910 Chestnut St.

1908. Fox, Herbert, M.D., Director of the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania; Pathologist to the Laboratory of Comparative Pathology of the Zoölogical Society of Philadelphia; Pathologist to the Rush Hospital; Pathologist to the Children's Hospital. 3902 Locust St.

†1885. Fox, Joseph M., M.D. Torresdale, Pa.

1906. Fraley, Frederick, Jr., A.B., M.D. Overbrook, Pa.

1897. Frazier, Charles H., A.B., M.D., Sc.D., John Rhea Barton Professor of Surgery, University of Pennsylvania. 3600 Walnut St.

ELECTED

1916. Funk, Elmer Hendricks, M.D., Assistant Professor of Medicine in the Jefferson Medical College; Medical Director and Physician-in-Charge of the Department for Diseases of the Chest of Jefferson Hospital; Assistant Physician to the Pennsylvania Hospital; Visiting Physician to the White Haven Sanatorium. 1318 Spruce St.

1899. Gamble, Robert, G. M.D., one of the Attending Physicians to the Bryn Mawr Hospital. Haverford, Pa.

1912. Gaskill, Henry Kennedy, M.D. S. E. Cor. Nineteenth and Spruce Sts.

1917. Gerhard, Arthur Howell, M.D. 1615 N. Delaware Ave.

1902. Ghriskey, Albert A., M.D. 3936 Walnut St.

1899. Gibbon, John H., M.D., Professor of Surgery in the Jefferson Medical College; Surgeon to the Pennsylvania Hospital and Consulting Surgeon to the Bryn Mawr Hospital. 1608 Spruce St.

1920. Gill, A. Bruce, A.B., M.D., Professor of Orthopædic Surgery, University of Pennsylvania; Surgeon to the Orthopædic Hospital; Orthopædic Surgeon to the Presbyterian Hospital; Chief Surgeon to the Widener Memorial Industrial Training School for Crippled Children. The Lenox, Thirteenth and Spruce Sts.

*1913. Ginsburg, Nathaniel, M.D. 10 Peterboro Ave., Detroit, Mich.

1897. Girvin, John H., M.D., Gynecologist to the Presbyterian Hospital; Associate Professor of Gynecology, Graduate School of Medicine, University of Pennsylvania. 2120 Walnut St.

1920. Githens, Thomas Stotesbury, M.D. Hamilton Court, Thirty-ninth and Chestnut Sts.

1906. Gittings, J. Claxton, M.D., Professor of Pediatrics, School of Medicine and Graduate School of Medicine, University of Pennsylvania; Visiting Physician to the Children's Hospital of Philadelphia. 1828 Pine St.

1905. Given, Ellis E. W., M.D., Surgeon to the Philadelphia Freemasons Memorial Hospital of the Masonic Home, Elizabethtown, Pa.; Surgeon to the Dispensary of the Episcopal Hospital. 2714 Columbia Ave.

1894. Gleason, E. B., S.B., M.D., LL.D., Professor of Otology in the Medico-Chirurgical College. 2033 Chestnut St.

ELECTED

1906. Goepp, R. Max, M.D., Professor of Medicine, Graduate School of Medicine, University of Pennsylvania. 1814 Spruce St.

1906. Goldberg, Harold G., M.D., Ophthalmic Surgeon to the Episcopal and Misericordia Hospitals, Kensington Hospital for Women and Baltimore and Ohio Railroad. 2213 Walnut Street.

1908. Goodman, Edward H., M.D., Associate in Medicine in the University of Pennsylvania; Consultant to the Medical Dispensary of the University Hospital; Assistant Physician to the University Hospital; Assistant Physician to the Philadelphia General Hospital; Physician to the Presbyterian Hospital. 248 S. Twenty-first St.

1905. Gordon, Alfred, M.D., Neurologist to the Mt. Sinai, the Northwestern General, and the Douglass Memorial Hospitals. 1812 Spruce St.

1894. Graham, Edwin E., M.D., Professor of Pediatrics in the Jefferson Medical College; Pediatrist to the Jefferson and the Philadelphia General Hospitals; Physician to the Franklin Reformatory Home. 1713 Spruce St.

1904. Grayson, Charles P., M.D., Professor of Laryngology and Rhinology in the University of Pennsylvania; Physician-in-Charge of the Throat and Nose Department of the University Hospital; Otolaryngologist to the Philadelphia General Hospital. 262 S. Fifteenth St.

1910. Greenman, Milton J., M.D., Sc.D., Director of the Wistar Institute of Anatomy and Biology. Wistar Institute of Anatomy and Biology, Thirty-sixth St. and Woodland Ave.

1883. Griffith, J. P. Crozer, A.B., M.D., Ph.D., Professor of Pediatrics in the University of Pennsylvania; Corresponding Member of the Société de Pédiatrie de Paris; Physician to the Children's Hospital of Philadelphia. 1810 Spruce St.

1912. Griscom, J. Milton, B.S., M.D., Assistant Surgeon to the Wills Hospital. 2213 Walnut St.

1911. Gummey, Frank Bird, M.D., Visiting Physician to the Germantown Hospital and Dispensary; Visiting Physician to the Midnight Mission. 5418 Greene St., Germantown.

*1902. Gwyn, Norman B., M.D., Clinician in Medicine, Toronto General Hospital; Clinician in Medicine, Medical Faculty, University of Toronto School. 48 Bloor St., E., Toronto, Canada.

1894. Hamill, Samuel McC., M.D., Professor of Diseases of Chil-

ELECTED

dren in the Philadelphia Polyclinic and College for Graduates in Medicine; Pediatrist to the Presbyterian Hospital; Pediatrist to St. Vincent's Home. 1822 Spruce St.

1897. HAND, ALFRED, JR., M.D., Professor of Pediatrics, Graduate School of Medicine, University of Pennsylvania; Visiting Physician to the Children's Hospital, to the Children's Hospital of the Mary J. Drexel Home and to the Methodist Hospital. 1724 Pine St.

1886. HANSELL, HOWARD F., M.D., Professor of Ophthalmology in the Jefferson Medical College; Ophthalmic Surgeon to the Philadelphia General Hospital and to the Jefferson Medical College Hospital; Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic. N. E. Cor. Seventeenth and Walnut Sts.

1889. HARE, HOBART A., M.D., LL.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College. 1801 Spruce St.

1903. HART, CHARLES D., A.M., M.D., Inspector and Secretary of the Eastern State Penitentiary; National Executive Committee and Chairman of the Philadelphia Committee, Boy Scouts of America. Chestnut Hill.

‡1885. HARTE, RICHARD H., M.D. (Hon.), F.R.C.S. Ireland; Adjunct Professor of Surgery in the University of Pennsylvania; Surgeon to the Pennsylvania and the Orthopædic Hospitals; Consulting Surgeon to St. Mary's, Memorial and the Bryn Mawr Hospitals. 1503 Spruce St.

*1888. HARTZELL, MILTON B., A.M., M.D., LL.D., Professor of Dermatology in the University of Pennsylvania. Fayetteville, Pa.

1907. HATFIELD, CHARLES JAMES, A.B (Princeton), M.D., Executive Director of the Henry Phipps Institute for the Study, Treatment, and Prevention of Tuberculosis; Visiting Physician to the White Haven Sanatorium. Phipps Institute, Seventh and Lombard Sts.

‡1872. HAYS, I. MINIS, M.D. 266 S. Twenty-first St.

1911. HEED, CHARLES R., M.D., Ophthalmologist to Girard College; Assistant Ophthalmologist to the Jefferson Medical College Hospital. 1205 Spruce St.

1908. HEINEBERG, ALFRED, P.D., M.D., Associate in Gynecology in the Jefferson Medical College; Assistant Gynecologist to St. Agnes' Hospital. 1923 Spruce St.

1901. HEISLER, JOHN C., M.D., Professor of Anatomy, University of Pennsylvania. 3829 Walnut St.

ELECTED

1903. Henry, J. Norman, M.D., Physician to the Pennsylvania Hospital; Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania; Assistant Physician to the Philadelphia General Hospital. 1906 Spruce St.

1891. Hewson, Addinell, A.B., A.M., M.D., Professor of Anatomy in the Philadelphia Polyclinic and College for Graduates in Medicine; Professor of Anatomy and Histology in the Temple University; Surgeon to Memorial Hospital, Roxborough. 326 S. Fifteenth St.

1924. Hewson, William, A.B., M.D., Instructor in Cardiology, Graduate School of Medicine, University of Pennsylvania; Acting Chief of Cardiac Clinic, Presbyterian Hospital; Dispensary Physician, Bryn Mawr Hospital; Laryngologist, Pennsylvania Institution for Instruction of Blind. 6300 Overbrook Ave.

1909. Higbee, William S., M.D., President of the Pennsylvania State Board of Examiners for Registration of Nurses. 5121 Pine St.

1897. Hinkle, William M., M.D., Lecturer on the Anatomy and Physiology of the Vocal Organs in the National School of Elocution and Oratory. 923 N. Sixty-fourth St.

*1892. Hinsdale, Guy, A.M., M.D. Hot Springs, Virginia.

*1888. Hirsh, A. Bern, M.D., Consulting Physician for Physiotherapy, Beth Israel Hospital. 67 W. Ninety-fourth St., New York City.

1888. Hirst, Barton Cooke, A.B., M.D., LL.D., Professor of Obstetrics in the University of Pennsylvania; Gynecologist to the Philadelphia General and the Howard Hospitals. 1821 Spruce St.

‡1903. Hirst, John Cooke, M.D., Associate Professor of Gynecology, Graduate School of Medicine, University of Pennsylvania; Associate in Obstetrics, School of Medicine, University of Pennsylvania; Obstetrician-in-Chief, St. Agnes' Hospital; Gynecologist-in-Chief to Mt. Sinai Hospital. 1823 Pine St.

1924. Hirst, John C., 2nd, A.B., M.D., Instructor in Obstetrics, School of Medicine, University of Pennsylvania; Assistant Obstetrican, Philadelphia General and Howard Hospitals; Assistant Surgeon, Department of Obstetrics, University Hospital. 1918 Pine St.

*1908. Hitchens, Arthur Parker, M.D., Instructor in Bacteriology, Army Medical School; Special Lecturer, Infection and Immunity, Graduate School, Department of Agriculture; Advisory Professor in Bacteriology, American University. Washington, D. C.

ELECTED

1924. Hitschler, William A., M.D., Professor of Rhinology, Temple University. 1635 Spruce St.

1905. Hodge, Edward Blanchard, A.B., M.D., Surgeon to the Presbyterian and the Germantown Hospitals; Associate Surgeon to the Pennsylvania Hospital; Associate Surgeon to the Widener Memorial Training School. 2019 Spruce St.

1913. Hoffman, Clarence, M.D., 1630 Pine St.

1906. Holloway, Thomas B., M.S., M.D., Vice-Dean for and Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Instructor in Ophthalmology in the University of Pennsylvania; Attending Surgeon to the Wills Hospital; Ophthalmologist to the Pennsylvania Institution for the Instruction of the Blind at Overbrook. 1819 Chestnut St.

1914. Hooker, Richard S., M.D. 2147 N. Howard St.

1919. Hopkins, Arthur H., B.S. (Haverford), M.D. 1726 Pine St.

1925. Hopkinson, R. Dale, M.D., Registrar and Assistant Physician, Abington Memorial Hospital. Jenkintown, Pa.

1908. Hoyt, Daniel M., M.D., Assistant Visiting Physician to the Philadelphia General Hospital. The Tracy, Thirty-sixth and Chestnut Sts.

*1912. Huber, G. Carl, M.D., Professor of Anatomy and Director of the Anatomic Laboratories in the University of Michigan. 1330 Hill St., Ann Arbor, Mich.

1892. Hughes, William E., M.D., Visiting Physician to the Philadelphia General Hospital; Consulting Physician to the Presbyterian Hospital. 3945 Chestnut St.

1923. Hume, John E., A.B., M.D., Visiting Physician, Medical Department, Howard Hospital. N. E. Cor. Twentieth and Chestnut Sts.

1912. Hunter, John W., B.S., M.D. McDaniel, Md.

1921. Hunter, Robert J., M.D., Laryngologist, Philadelphia General Hospital; Chief of Dispensary and Assistant Laryngologist and Aurist, Howard Hospital; Instructor in Otology, University of Pennsylvania, Graduate School. 2011 Chestnut St.

1898. Hutchinson, James P., M.D., Surgeon to the Pennsylvania, the Methodist, the Children's, Memorial and the Bryn Mawr Hospitals; Adjunct Professor of Surgery in the University of Pennsylvania. Penn Mutual Life Insurance Company, Sixth and Walnut Sts.

1921. Ivy, Robert H., D.D.S., M.D., Professor of Clinical Maxillo-

ELECTED

Facial Surgery, University of Pennsylvania; Oral Surgeon to the Hospitals of the Graduate School of Medicine, University of Pennsylvania and to the Philadelphia General Hospital; Consultant in Maxillo-Facial Surgery, Walter Reed General Hospital, Washington, D. C. 1503 Medical Arts Building.

1917. JACKSON, CHEVALIER, M.D., Sc.D., Professor of Laryngology, Jefferson Medical College; Professor of Bronchoscopy and Esophagoscopy, Graduate School of Medicine, University of Pennsylvania. 128 S. Tenth St.

*1885. JACKSON, EDWARD, A.M., M.D., Sc.D., Emeritus Professor of Ophthalmology in the University of Colorado; Emeritus Professor of Diseases of the Eye in the Philadelphia Polyclinic. 217 Imperial Bldg., Denver, Colo.

*1906. JACOBS, FRANCIS BRINTON, B.S., M.D., Pediatrist to the Chester County Hospital. West Chester, Pa.

1922. JAMESON, HOWARD LEON, M.D., Assistant Professor of Medicine, Graduate School of Medicine, University of Pennsylvania; Assistant Physician, Medico-Chirurgical and Polyclinic Hospitals. 2133 S. Sixteenth St.

1920. JANVIER, G. VICTOR, M.D., Instructor in Obstetrics, University of Pennsylvania; Assistant Obstetrician to the Philadelphia General Hospital and the University of Pennsylvania Hospital; Associate in Gynecology at the American Stomach Hospital. Lansdowne, Pa.

1913. JEFFERYS, WILLIAM HAMILTON, A.B., A.M., M.D. Rosemont, Pa.

1919. JENKS, HORACE H., A.B., M.D., Medical Director, Associated Medical Clinics; Physician to the Out-Patient Department, Children's Hospital; Instructor in Pediatrics, Graduate School of Medicine, University of Pennsylvania. 918 Clinton Street.

1898. JOHNSON, RUSSELL H., A.B. (Princeton), M.D., Physician to the Pennsylvania Institution for the Deaf and Dumb. Chestnut Hill, Philadelphia.

1918. JONAS, LEON, M.D. 2253 N. Seventeenth St.

1900. JONES, CHARLES JAMES, A.M., M.D., LL.D., Ophthalmic Surgeon to St. Joseph's Hospital; Ophthalmic Surgeon to the House of the Good Shepherd, Germantown; Consulting Ophthalmologist to St. Vincent's Home. 256 S. Fifteenth St.

ELECTED

1924. Jones, Harold W., M.D., Demonstrator of Medicine, Jefferson Medical College; Assistant Physician, Philadelphia General Hospital. 1426 Spruce St.

1913. Jones, John F. X., B.S., A.B., A.M., M.D., Surgeon to St. Joseph's, Misericordia and St. Agnes' Hospitals. 103 S. Twenty-first St.

1900. Jopson, John H., M.D., Professor of Clinical Surgery, University of Pennsylvania; Professor of Surgery, Graduate School of Medicine, University of Pennsylvania; Surgeon to the Presbyterian and the Children's Hospitals. 1824 Pine St.

1900. Judson, Charles F., A.B., M.D., Physician to Out-patient Department of the Lankenau Hospital and to the Southern Home for Children. 1005 Spruce St.

1902. Jump, Henry D., M.D., Professor of Applied Therapeutics and Clinical Medicine, Woman's Medical College; Physician to Philadelphia General and Misericordia Hospitals. 2019 Walnut St.

‡1886. Jurist, Louis, M.D. 1308 N. Broad St.

1903. Kalteyer, Frederick J., M.D., Associate Professor of Medicine, Jefferson Medical College; Assistant Physician, Jefferson Medical College Hospital; Consulting Physician to the Pottstown Hospital, Pottstown, Pa. 1530 Locust St.

*1910. Karsner, Howard T., M.D., Professor of Pathology in the Western Reserve University Medical School. 2109 Adelbert Rd., Cleveland, Ohio.

1923. Kay, James, M.D., Visiting Physician, Episcopal Hospital; Assistant Instructor of Medicine, Jefferson Medical College. 600 W. Olney Ave.

1920. Keating, Peter McCall, M.D., Chief of Surgical Dispensary, St. Agnes Hospital; Assistant Attending Surgeon, Bryn Mawr Hospital; Assistant, Surgical Out-patient Department, Pennsylvania Hospital; Pathologist, Chester County Hospital. Medical Arts Bldg., San Antonio, Texas.

1924. Keeler, J. Clarence, M.D., Associate Professor of Otology, Jefferson Medical College and Hospital; Assistant in Oto-laryngology, Germantown Hospital; Consultant Oto-laryngologist, Pottstown Hospital, Pa., and Newcombe Hospital, Vineland, N. J. Medical Arts Building.

†1867. Keen, William W., M.D., LL.D. (Hon.), Ph.D. (Upsala) (Hon.), Sc.D. (Jefferson and Harvard), Dr., Honoris Causa, University of Paris; (Hon.) F.R.C.S. (Eng., Edin. and Ireland), Emeritus Professor of Surgery, Jefferson Medical

ELECTED

College; Hon. Foreign Associate, Paris Academy of Medicine; Hon. Foreign Member, Paris Surgical Society and Belgian Surgical Society and the Royal Academy of Medicine of Belgium; Hon. Foreign Member, Royal Society of Medicine, London. 1520 Spruce St.

1912. Keene, Floyd E., M.D., Instructor in Gynecology in the University of Pennsylvania; Assistant Gynecologist to the University Hospital; Gynecologist to the Chestnut Hill Hospital. Medical Arts Building.

1913. Kelly, Francis Joseph, M.D. 2035 Chestnut St.

*1887. Kelly, Howard A., A.B., M.D., LL.D. (Aberdeen, Wash. and Lee, and Univ. of Pa.), Professor of Gynecology in Johns Hopkins University and Gynecologist to the Johns Hopkins Hospital, Baltimore, Md.; Hon. Fellow of the Edinburgh Obstetrical Society, the Royal Academy of Medicine of Ireland, and of the Glasgow Obstetrical and Gynecological Society. 1418 Eutaw Place, Baltimore, Md.

1909. Kelly, James A., A.M., M.D., Visiting Surgeon to St. Mary's and Memorial Hospitals; Associate in Surgery in the Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Visiting Surgeon to St. Joseph's Hospital. 1815 Spruce St.

1912. Kelly, Thomas C., A.M., M.D., Associate in Medicine, University of Pennsylvania; Assistant Professor of Medicine, Graduate School, University of Pennsylvania; Pediatrist to St. Christopher, Misericordia and St. Mary's Hospitals; Assistant Physician, Philadelphia General Hospital. 105 School Lane, Germantown.

1898. Kempton, Augustus F., M.D. 2118 Pine St.

1905. Kercher, Delno E., M.D. 1534 Pine St.

1921. Kern, Richard A., A.B., M.D., Associate in Medicine, University of Pennsylvania; Assistant Physician, University Hospital; Associate in Medicine, Graduate School of Medicine, University of Pennsylvania. 906 Medical Arts Building.

1920. Klauder, Joseph Victor, A.B., M.D., Professor of Dermatology, Woman's Medical College; Associate Professor, Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania; Dermatologist, Misericordia, Woman's Medical College and American Stomach Hospitals; Assistant Dermatologist, Philadelphia General Hospital. 1934 Spruce Street.

ELECTED

1920. Klein, Thomas, M.D., Associate Professor of Medicine, Graduate School, University of Pennsylvania; Assistant Physician, Presbyterian Hospital. 250 S. Eighteenth St.

1913. Klopp, Edward J., M.D., Instructor in Surgery in the Jefferson Medical College; Assistant Surgeon to the Germantown Hospital; Chief Clinical Assistant in the Surgical Department of the Jefferson Hospital; Assistant Surgeon to the Out-patient Department of the Pennsylvania Hospital. 1611 Spruce St.

1895. Kneass, Samuel S., M.D., Associate in the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania. 1510 Walnut St.

1908. Knipe, Jay C., M.D., Ophthalmologist to the Jewish Hospital; Assistant Ophthalmologist to the Philadelphia General Hospital and to the Mary J. Drexel Home; Chief of the Eye Clinic at the Jefferson Medical College Hospital; Demonstrator of Osteology and Syndesmology in the Jefferson Medical College. 2035 Chestnut St.

1919. Knipe, Norman Leslie, Ph.B. (Cornell); M.D., Instructor in Obstetrics, University of Pennsylvania; Assistant Obstetrician, University Hospital; Gynecologist, St. Mary's Hospital; Associate Gynecologist, American Stomach Hospital. 2018 Chestnut St.

1908. Knowles, Frank Crozer, M.D., Professor of Dermatology, Jefferson Medical College; Dermatologist to the Presbyterian and Children's Hospitals; Chief of Clinic, Pennsylvania Hospital. 2022 Spruce St.

1925. Knox, Harry E., M.D., Assistant Surgeon, Germantown Hospital and Dispensary; Assistant Attending Surgeon, St. Christopher's Hospital for Children; Gynecologist, Out-patient Department, Lankenau Hospital. 719 Sixty-sixth Ave., Oak Lane, Phila.

1914. Kolmer, John A., M.D., Dr. P.H., M.Sc., Professor of Pathology and Bacteriology, Graduate School of Medicine, University of Pennsylvania; Head of the Department of Pathology and Bacteriology in the Dermatological Research Laboratories of Philadelphia; Consulting Pathologist to St. Vincent's and Misericordia Hospitals; Consulting Serologist to Memorial and Germantown Hospitals. Cynwyd, Pa.

1904. Krauss, Frederick, M.D., Ophthalmic Surgeon to the Episcopal Hospital; Ophthalmic Surgeon to St. Christopher's Hospital for Children; Laryngologist to the Abington Hospital. 1701 Chestnut St.

ELECTED

1914. Krumbhaar, Edward B., A.B., Ph.D., M.D., Director of Laboratories, Philadelphia General Hospital; Associate Professor of Pathology, Graduate School of Medicine, University of Pennsylvania. Box 4310, Chestnut Hill.

1900. Krusen, Wilmer, M.D., Professor of Gynecology in the Medical Department of Temple University; Chief Gynecologist to the Samaritan and the Garretson Hospitals; Consulting Gynecologist to the Charity and Mercy Hospitals. 127 N. Twentieth St.

*1909. Laird, J. Packard, M.D. 483 N. E. Twenty-seventh St., Miami, Florida.

1904. Landis, Henry R. M., M.D., Director of the Clinical and Sociological Departments of the Henry Phipps Institute of the University of Pennsylvania; Visiting Physician to the White Haven Sanatorium. 1817 Pine St.

1907. Langdon, H. Maxwell, M.D., Associate Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Instructor of Ophthalmology, Under-Graduate School, University of Pennsylvania; Ophthalmologist of the Presbyterian, Orthopædic and Children's Hospitals. 1530 Locust St.

1922. Lawrance, Stuart J., M.D., Obstetrician, St. Mary's Hospital. 1332 Spruce St.

1922. Leach, Wilmon W., M.D., Physician to Dispensary, Children's Hospital. 2118 Spruce St.

1920. Leavitt, Frederick Headley, M.D. 1527 Pine St.

1904. Le Boutillier, Theodore, M.D., Assistant Professor, Epidemic Contagious Diseases, Graduate School of Medicine, University of Pennsylvania; Senior Pediatrist, Philadelphia Hospital for Contagious Diseases; Visiting Physician, Babies' Hospital, North Philadelphia. 2017 Spruce St.

1908. Lee, Walter Estell, M.D., Surgeon to the Germantown, Children's, Pennsylvania and Bryn Mawr Hospitals and the Associated Medical Clinics; Associate Professor of Surgery, Graduate School of Medicine, University of Pennsylvania; Consulting Surgeon, Chester County Hospital, West Chester, Pa. 905 Pine St.

1903. Leffmann, Henry, A.M., M.D., D.D.S., Ph.D., Honorary Professor of Chemistry, Wagner Free Institute of Science; Emeritus Pathological Chemist, Jefferson Hospital; Lecturer on Research, Philadelphia College of Pharmacy and Science. 1729 N. Seventeenth St.

ELECTED

1892. Leidy, Joseph, M.D., Officier d'instruction publique, France; Consulting Physician to the Pennsylvania Training School for Feeble-minded Children. 1713 Walnut St.

1920. Leopold, Simon S., M.D., Instructor in Medicine, University of Pennsylvania; Assistant in Medicine, University Hospital. 2025 Spruce St.

1915. Lewis, Fielding O., M.D., Associate in Laryngology in the Jefferson Medical College Hospital; Operating Clinical Chief of the Laryngological Dispensary and Clinical Assistant of the Otological Dispensary of the Jefferson Medical College Hospital; Laryngologist of the Philadelphia General Hospital. 261 S. Seventeenth St.

1877. Lewis, Morris J., M.D., Attending Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases and Emeritus Physician to the Pennsylvania Hospital. 1820 Pine St.

*1911. Lewis, Paul A., M.D. Princeton, N. J.

1904. Lindauer, Eugene, M.D., Assistant Neurologist to the Philadelphia General and Polyclinic Hospitals; Instructor in Nervous Diseases, Graduate School of Medicine, University of Pennsylvania. 6451 N. Broad St.

1886. Lloyd, J. Hendrie, A.M. (Princeton), M.D., Neurologist to the Philadelphia General Hospital and to the Methodist Episcopal Hospital; Consulting Neurologist to the State Asylum for the Chronic Insane at Wernersville, and to the Pennsylvania Training School for Feeble-minded Children at Elwyn. 4057 Spruce St.

1907. Lodholz, Edward, M.D., Isaac Ott Professor of Physiology, Graduate School of Medicine, University of Pennsylvania. Medical Laboratories, University of Pennsylvania.

1893. Longaker, Daniel, M.D., Obstetrician to the Kensington Hospital for Women and Visiting Obstetrician to the Jewish Maternity Hospital. 1806 Spruce St.

1907. Loux, Hiram R., M.D., Professor of Genito-urinary Surgery in the Jefferson Medical College; Surgeon to the Philadelphia General Hospital. Medical Arts Building, Sixteenth and Walnut Sts.

1921. Lucke, Baldwin, Dr. P.H., M.D., Assistant Pathologist, University and Philadelphia General Hospitals; Assistant Professor of Pathology, Medical School, University of Pennsylvania.

1924. Ludy, John B., A.B., A.M., M.D., Dermatologist, Lankenau and Methodist Hospitals; Assistant Dermatologist, Pennsyl-

ELECTED

vania, Episcopal and Philadelphia General Hospitals. Medical Arts Building.

1923. LUEDERS, CHARLES W., A.B., M.D., Biochemist, Pennsylvania Hospital for Mental and Nervous Diseases; Research Worker, Gastro-enterology, Jefferson Medical College. Medical Arts Building.

1919. LYNCH, FRANK B., JR., M.D., Dickson Fellow in Bacteriology to the Pepper Laboratory of Clinical Medicine, University of Pennsylvania; Serologist, University Hospital; Instructor in Pathology, Evans Institute, University of Pennsylvania. 6028 Columbia Ave.

1914. LYON, B. B. VINCENT, A.B. (Williams Coll.), M.D. (Johns Hopkins), Associate in Medicine, Jefferson Medical College; Chief-of-Clinic, Gastro-Intestinal Department, Jefferson Hospital; Visiting Physician to Methodist Hospital. 328 S. Twenty-first St.

1900. MCCARTHY, DANIEL J., M.D., Professor of Medical Jurisprudence (George B. Wood Foundation) in the University of Pennsylvania; Neurologist to the Philadelphia General and St. Agnes' Hospitals, and to the Henry Phipps Institute. 2025 Walnut St.

1913. MCCRAE, THOMAS, B.A., M.D., F.R.C.P. (Lond.), Professor of Medicine in the Jefferson Medical College; Physician to the Jefferson and Pennsylvania Hospitals. 1929 Spruce Street.

1895. MCFARLAND, JOSEPH, M.D., Sc.D., Professor of Pathology and Bacteriology in the Medical Department of the University of Pennsylvania; Pathologist to the Philadelphia General Hospital. 442 W. Stafford St., Germantown.

1905. MCKENZIE, R. TAIT, M.D., LL.D., Professor of Physical Education and Director of the Department of Physical Education in the University of Pennsylvania. 2014 Pine St.

*1916. MCKNIGHT, HOWARD A., A.B., M.D. 232 Bushnell Annex, Springfield, Ohio.

1915. MCLEAN, JOHN D., M.D. 4316 Chestnut St.

1924. MCMILLAN, THOMAS M., A.B., M.D., Assistant Physician, Pennsylvania Hospital; Cardiologist, Philadelphia General Hospital; Assistant Instructor in Medicine, School of Medicine, University of Pennsylvania; Instructor in Medicine, Graduate School of Medicine, University of Pennsylvania. 2044 Locust St.

ELECTED

1924. McPhedran, F. Maurice, A.B., M.D., Assistant in Clinical Research, Henry Phipps Institute. Seventh and Lombard Sts.

*1900. McReynolds, Robert Phillips, M.D. 213 S. Broadway, Los Angeles, Calif.

1910. Mackinney, William H., M.D., Assistant Surgeon to the Dispensary for Genito-urinary Diseases, University Hospital; Assistant in the Urological Dispensary of the Lankenau Hospital. 1701 Chestnut St.

1901. MacLeod, George I., M.D. Ardmore, Pa.

1914. Maier, F. Hurst, M.D., Associate in Gynecology to the Jefferson Medical College; Gynecologist to St. Joseph's Hospital; Gynecologist, Obstetrician and Consultant, Prenatal Clinic, Philadelphia General Hospital; Associate Gynecologist, St. Mary's Hospital. 2019 Walnut St.

1913. Major, Charles P., B.S., M.D., Physician to the Dispensary of the Germantown Hospital; Pediatrist to the Dispensary of the Germantown Hospital; Pediatrist to the Abington Memorial Hospital. Tenth and Oak Lane.

1913. Manges, Willis F., M.D., Roentgenologist to the Jefferson Hospital; Director of the Roentgen-ray Laboratory in the Philadelphia General Hospital. 235 S. Fifteenth St.

1898. Marshall, George Morley, M.D., Laryngologist to the Philadelphia General Hospital; Laryngologist and Otologist to St. Joseph's Hospital. 1819 Spruce St.

1889. Martin, Edward, M.D., Professor of Surgical Physiology, University of Pennsylvania. 135 S. Eighteenth St.

*1911. Meigs, Edward Browning, A.B., M.D., Physiologist in the Dairy Division of the United States Department of Agriculture. 1445 Rhode Island Ave., N. W., Washington, D. C.

1914. Mencke, J. Bernhard, A.B., M.D., Assistant Surgeon to the Lankenau Hospital; Surgeon to the Out-patient Department of the Lankenau Hospital. 1816 Spruce St.

1923. Mendelson, Walter, M.D. 639 Church Lane, Germantown.

1914. Merrill, William Jackson, A.B., M.D., Associate Professor of Orthopædic Surgery, Graduate School of Medicine, University of Pennsylvania; Orthopædic Surgeon to the Children's Hospital, Germantown Hospital, Children's Seashore House; Consulting Orthopædic Surgeon to the Howard Hospital and Glen Mills School. 2017 Spruce St.

*1894. Miller, D. J. Milton, M.D., Associate Physician to the Children's Hospital, Philadelphia; Pediatrist to the Bamberger Home for Invalid Children, Longport, N. J. N. W. Cor. Pacific and California Aves., Atlantic City, N. J.

ELECTED

1922. Miller, Edwin B., M.D., Assistant Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Associate in Ophthalmology, Temple University; Ophthalmologist, Roosevelt Hospital. 2008 Walnut St.

1921. Miller, T. Grier, A.B., M.D., Assistant Physician, University Hospital; Associate in Medicine, University of Pennsylvania. 110 S. Twentieth St.

1881. Mills, Charles K., M.D., LL.D., Emeritus Professor of Neurology in University of Pennsylvania; Neurologist to Philadelphia General Hospital; Consulting Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases. 2121 DeLancey St.

*1917. Mitchell, A. Graeme, M.D., Professor of Pediatrics, University of Cincinnati; Director of Pediatric Service, Cincinnati General Hospital; Dean of Staff of Children's Hospital, Cincinnati. Cincinnati General Hospital.

1904. Mitchell, Charles F., M.D., Surgeon to the Pennsylvania, Bryn Mawr, and Germantown Hospitals. 2003 Pine St.

1921. Mohler, Henry K., P.D., M.D., Associate in Medicine, Jefferson Medical College; Medical Director, Jefferson Hospital. 319 S. Sixteenth St.

*1908. Montgomery, Charles M., A.B., M.D., St. Joseph's Sanatorium, Asheville, N. C.

1882. Montgomery, Edward E., A.M., M.D., LL.D., Emeritus Professor of Gynecology, Jefferson Medical College and Gynecologist to St. Joseph's Hospital, Retired. Veree Road, Fox Chase.

1923. Moore, William F., M.D., Assistant, Bronchoscopic Clinic, Jefferson Hospital; Bronchoscopist to Philadelphia General Hospital and Philadelphia Hospital for Contagious Diseases; Assistant Laryngologist, Children's Hospital, Out-patient Department; Laryngologist to Tuberculosis Department, Philadelphia General Hospital. 255 S. Sixteenth St.

1924. Moorhead, Stirling W., A.B., M.D., Associate in Urology, School of Medicine, University of Pennsylvania; Assistant Surgeon, Department of Genito-urinary Surgery and in Urological Dispensary, University Hospital; Urologist, Howard Hospital. 1523 Pine St.

1918. Morgan, Arthur C., M.D., Professor of Applied Therapeutics, Medical Department, Temple University; Visiting Physician to Tuberculosis Department, Philadelphia General Hospital; Physician-in-Chief to the Frankford Hospital. 2018 Chestnut St.

ELECTED

1886. Morris, Caspar, M.D. 2050 Locust St.

1893. Morris, Elliston J., M.D., Physician to the Episcopal Hospital. 128 S. Eighteenth St.

1883. Morris, Henry, M.D., Emeritus Professor of Anatomy in the Woman's Medical College of Pennsylvania; Consulting Physician to St. Joseph's Hospital. 2310 Pine St.

1897. Morton, Samuel W., M.D. Aldine Hotel.

1905. Müller, George P., M.D., Professor of Clinical Surgery, University of Pennsylvania; Surgeon to the University and Misericordia Hospitals. 1930 Spruce St.

*1915. Musser, John H., Jr., B.S., M.D., Professor of Medicine and Head of Department, School of Medicine, Tulane University of Louisiana. 1551 Canal St., New Orleans, La.

1905. Mutschler, Louis H., M.D., Surgeon to the Episcopal Hospital; Assistant Surgeon to the Orthopædic Hospital. 1625 Spruce St.

*1896. Myers, T. D., M.D. 831 University Ave., Palo Alto, Calif.

1902. Nassau, Charles F., M.D., LL.D., Associate Professor of Surgery in the Jefferson Medical College; Surgeon to St. Joseph's Hospital; Chief Surgeon to the Frankford Hospital; Surgeon to Mount Sinai Hospital. 1710 Locust St.

1886. Neff, Joseph S., A.M., M.D., LL.D., D.P.H., Narberth, Pa.

1887. Neilson, Thomas Rundle, A.M., M.D., Surgeon Emeritus to the Episcopal Hospital; Consulting Surgeon to St. Christopher's Hospital for Children; Emeritus Professor of Genito-urinary Surgery in the University of Pennsylvania. 1937 Chestnut St.

1905. Newcomet, William S., M.D., Physician in Charge of Radiological Department, Jefferson, Presbyterian and Oncologic Hospitals. 3501 Baring St.

1905. Newlin, Arthur, B.S., M.D., Physician to the Pennsylvania Hospital; Physician to the Dispensary of the Children's Hospital; Assistant Physician to the Orthopædic Hospital. 1804 Pine St.

1899. Nicholson, William Rufus, A.B., M.D., Professor of Gynecology, Graduate School of Medicine, University of Pennsylvania; Attending Gynecologist and Attending Obstetrician to the Methodist Episcopal Hospital; Attending Obstetrician to the Presbyterian Hospital. 2023 Spruce St.

1889. Noble, Charles P., M.D., Sc.D. (Hon.), Formerly Surgeon-in-Chief, Kensington Hospital for Women; Formerly Clinical Professor of Gynecology, Woman's Medical College. Radnor, Pa.

ELECTED

1905. NORRIS, CHARLES C., M.D., Associate in Gynecology, University of Pennsylvania Medical School; Assistant Professor, Graduate School of Medicine, University of Pennsylvania; Assistant Gynecologist to the Hospital of the University of Pennsylvania; Gynecologist to the Children's Hospital, Philadelphia; Gynecologist and Obstetrician, Philadelphia General Hospital. Coronado, Twenty-second and Chestnut Streets.

1905. NORRIS, GEORGE WILLIAM, A.B., M.D., Professor of Clinical Medicine in the University of Pennsylvania; Physician-in-Chief, Medical Service "A", Pennsylvania Hospital; Attending Specialist (Heart and Lungs), U. S. Public Health Service (Veterans' Bureau). 321 S. Eleventh St.

*1901. NORRIS, HENRY, M.D., Surgeon to the Rutherford Hospital. Rutherfordton, N. C.

1892. NORRIS, RICHARD C., M.D., Lecturer on Clinical and Operative Obstetrics in the University of Pennsylvania; Obstetrician in Charge of the Preston Retreat; Visiting Obstetrician to the Philadelphia General Hospital; Gynecologist to the Methodist Episcopal Hospital, and Consulting Obstetrician and Attending Gynecologist to the Southeastern Dispensary and Hospital. 500 N. Twentieth St.

1913. O'NEAL, ALEXANDER H., A.B., A.M., M.D., Physician to the Cathcart and Richardson Homes, Devon; Anesthetizer to the Bryn Mawr Hospital. St. Davids, Pa.

1924. OPIE, EUGENE L., A.B., M.D., Professor of Experimental Pathology, University of Pennsylvania; Director of Laboratories, Henry Phipps Institute. 2203 St. James Place.

1920. OSTHEIMER, ALFRED J., A.B., M.D., L.R.C.P. (London), M.R.C.S. (England), Medical Director, Mental Hygiene Division, Public Charities Association of Pennsylvania; Consulting Neurologist, State Hospital, Norristown, Pa. Jenkintown, Pa.

1903. OSTHEIMER, MAURICE, A.B., M.D., Assistant Professor of Pediatrics in the University of Pennsylvania; Physician-in-Charge of the Children's Dispensary and Assistant Visiting Physician, Children's Ward, University Hospital. Whitford, Pa.

1913. OUTERBRIDGE, GEORGE W., A.B., M.D., Associate Professor of Gynecology, Graduate School of Medicine, University of Pennsylvania; Assistant Gynecologist to the Methodist Hospital; Gynecologist to the Abington Memorial Hospital. 1927 Spruce St.

ELECTED

1915. Owen, Hubley R., M.D., Professor of Clinical Surgery, Woman's Medical College; Surgeon, Philadelphia General Hospital; Assistant Surgeon, Orthopædic Hospital; Chief Surgeon, Bureaus of Police and Fire, Philadelphia. 319 S. Sixteenth St.

1897. Packard, Francis R., M.D., Chief of the Ear, Nose and Throat Service, Pennsylvania Hospital; Consulting Laryngologist and Aurist, Bryn Mawr Hospital; Consulting Aurist Chestnut Hill Hospital; Laryngologist, Children's Hospital of Philadelphia. 304 S. Nineteenth St.

1898. Page, Henry F., M.D., Assistant Physician to the Lankenau Hospital and Physician to the Medical Dispensary of the same; Clinical Professor of Medicine in the Woman's Medical College of Pennsylvania. 315 S. Sixteenth St.

1906. Pancoast, Henry K., M.D., Professor of Roentgenology in the University of Pennsylvania and Roentgenologist to the University Hospital. Ardmore, Pa.

1909. Parish, Benjamin D., B.S., M.D., Associate Professor in Otology, Graduate School of Medicine, University of Pennsylvania; Aurist and Laryngologist to St. Agnes' and Chestnut Hill Hospitals. 1927 Spruce St.

1899. Parke, William E., M.D., Consulting Obstetrician to the Episcopal Hospital; Associate Surgeon to the Kensington Hospital for Women; Gynecologist to the Frankford Hospital. 1739 N. Seventeenth St.

1925. Patten, Clarence A., M.D., Associate in Neurology, Graduate School of Medicine, University of Pennsylvania; Assistant Visiting Physician, Orthopædic Hospital; Assistant Neurologist and Chief of Neurological Clinic, Polyclinic Hospital; Assistant Neurologist, Philadelphia General Hospital. 2037 DeLancey St.

1910. Patterson, Ross Vernet, M.D., Dean and Associate Professor of Medicine, Jefferson Medical College; Physician to the Philadelphia General Hospital; Physician to the Protestant Episcopal Hospital; Assistant Physician to the Jefferson Hospital. 2126 Spruce St.

*1903. Pearce, Richard M., M.D., Sc.D., Director of Division of Medical Education, Rockefeller Foundation. 150 E. Seventy-third St., New York, N. Y.

1922. Pelouze, P. S., M.D., Associate in Urology, University of Pennsylvania; Surgeon-in-Charge, Urological Dispensary, University Hospital. Medical Arts Building.

ELECTED

1909. Pemberton, Ralph, M.S., M.D., Physician to the Presbyterian Hospital; Director of the Department of Clinical Chemistry in the Pathological Laboratory of the Presbyterian Hospital. 2120 Sansom St.

‡1889. Penrose, Charles Bingham, M.D., Ph.D. (Harvard), Formerly Professor of Gynecology in the University of Pennsylvania. 1720 Spruce St.

1914. Pepper, O. H. Perry, B.S., M.D., Assistant Professor of Medicine, University of Pennsylvania. Medical Arts Bldg.

†1902. Pepper, William, A.B., M.D., Dean of the School of Medicine, University of Pennsylvania; Member of the Council on Medical Education and Hospitals of the American Medical Association. University of Pennsylvania.

1916. Percival, Milton Fraser, M.D. 2332 S. Broad St.

1917. Peter, Luther C., A.M., M.D., Professor of Diseases of the Eye, Temple Medical School; Professor of Ophthalmology, University of Pennsylvania Graduate School. N. E. Cor. Twentieth and Chestnut Sts.

1912. Petty, Orlando H., B.S., A.M., M.D., Professor of Diseases of Metabolism, Graduate School of Medicine, University of Pennsylvania; Chief of the Department of Diseases of Metabolism, Hospitals of Graduate School of Medicine, University of Pennsylvania; Chief of Department of Metabolism, Philadelphia General Hospital. 1529 Pine St.

1905. Pfahler, George E., M.D., Assistant Radiologist, Medico-Chirurgical Hospital; Assistant Professor of Radiology, Graduate School of Medicine, University of Pennsylvania. 1321 Spruce St.

1915. Pfeiffer, Damon B., A.B., M.D., Assistant Professor of Surgery, Graduate School of Medicine, University of Pennsylvania; Surgeon, Methodist and Abington Memorial Hospitals; Assistant Surgeon, Presbyterian and Lankenau Hospitals. 1822 Pine St.

1907. Pfromm, George W., Ph.G., M.D., Assistant Physician to the American Stomach Hospital; Consulting Physician to the German Protestant Home for the Aged. 1431 N. Fifteenth St.

1907. Phillips, Horace, M.D., Assistant Surgeon, U. S. Public Health Service; Examining Physician, Office of the District Attorney. 905 Land Title Building.

1911. Piersol, George Morris, B.S., M.D., Professor of Medicine and Vice-Dean for Medicine, Graduate School of Medicine, University of Pennsylvania; Physician to the Philadelphia

ELECTED

General and Methodist Episcopal Hospitals. 1913 Spruce Street.

1917. PIPER, EDMUND BROWN, B.S., M.D., Associate in Obstetrics, University of Pennsylvania Medical School; Assistant Professor in Obstetrics, University of Pennsylvania Graduate School; Assistant Obstetrician to the University Hospital; Assistant Obstetrician and Gynecologist to the Philadelphia General Hospital. 1936 Spruce St.

1905. PITFIELD, ROBERT L., M.D., Pathologist to the Germantown Hospital; Bacteriologist to the Chestnut Hill Hospital for Lung Diseases. 5211 Wayne Ave.

1922. PLEASANTS, HENRY, JR., A.B., M.D., Assistant Visiting Physician, Chester County Hospital, West Chester, Pa.; Assistant in Neurological Clinic, Orthopædic Hospital. West Chester, Pa.

1896. POSEY, WILLIAM CAMPBELL, M.D., Ophthalmic Surgeon to the Howard Hospital; Consulting Ophthalmic Surgeon to the Wills Hospital; Chairman of the Commission on the Conservation of Vision for Pennsylvania. 2049 Chestnut St.

1899. POTTS, CHARLES S., M.D., Professor of Neurology, Graduate School of Medicine, University of Pennsylvania; Neurologist to the Philadelphia General Hospital; Consulting Neurologist, Lankenau Hospital; Consulting Neurologist, Hospital for the Insane, Atlantic County, New Jersey, 2018 Chestnut St.

*1907. PRICE, GEORGE E., M.D. Suite 620, Paulsen Bldg., Spokane, Wash.

1920. QUICKSALL, WILLIAM E., M.D. 1819 Spruce St.

1908. RADCLIFFE, MCCLUNEY, A.M. (Lafayette), M.D., LL.D., Consulting Ophthalmologist, Presbyterian Hospital; Attending Surgeon to the Wills Hospital. 1906 Chestnut St.

1913. RANDALL, ALEXANDER, A.M., M.D., Assistant Professor of Surgery in charge of the Department of Urology, University of Pennsylvania. 1306 Medical Arts Building.

1887. RANDALL, B. ALEX., M.A., M.D., Ph.D., Emeritus Professor of Otology in the University of Pennsylvania; Ear Surgeon to the Children's Hospital; Consulting Aurist to the Pennsylvania Institution for the Deaf and Dumb and to Memorial Hospital, Roxborough. 2009 Spruce St.

*1904. RAVENEL, MAZYCK P., M.D., Professor of Preventive Medicine and Bacteriology and Director of the Public Health Laboratory at the University of Missouri. 203 Hicks Ave., Columbia, Mo.

ELECTED

1925. Reeves, Rufus S., B.S., M.D., Associate in Medicine, Episcopal Hospital. 2227 Spruce St.

1920. Rehfuss, Martin E., M.D. N. E. Cor. 16th and Spruce Sts.

1921. Reiff, E. Paul, A.B., M.D., Member of Medical Staff, Methodist Episcopal Hospital. 5051 Chestnut St.

1919. Reimann, Stanley P., M.D., Director of the Research Institute, Lankenau Hospital; Assistant Professor of Experimental Pathology, Graduate School of Medicine, University of Pennsylvania. 516 Arbutus St., Germantown.

1923. Repplier, Sidney, J., M.D., Medical Director, Curtis Hospital, Curtis Publishing Company. Chestnut Hill, Phila.

‡1897. Rhein, John H. W., M.D., Professor of Nervous Diseases, Graduate School of Medicine, University of Pennsylvania; Neuropsychiatrist to the Philadelphia General Hospital; Consulting Neurologist to the Philadelphia Home for Incurables. 1732 Pine St.

1906. Rhein, Robert D., M.D., Chief Physician to the Clinic of the American Hospital for Diseases of the Stomach; Physician to the Philadelphia Home for Incurables; Examining Physician to the White Haven Sanatorium. S. W. Cor. Fifteenth and Pine Sts.

1891. Rhoads, Edward G., M.D., New Hope, Pa.

*1910. Rhoads, Samuel, M.D. Altadena, Calif.

1919. Richardson, Russell, A.M., M.D., Director of the Laboratory, Methodist Episcopal Hospital; Pathologist to Abington Memorial Hospital and the Associated Medical Clinics. 320 S. Sixteenth St.

1919. Ridpath, Robert F., M.D. 1737 Chestnut St.

1898. Riesman, David, M.D., Professor of Clinical Medicine, University of Pennsylvania; Visiting Physician to the Philadelphia General and University Hospitals; Consulting Physician to the Jewish and Woman's Hospitals. 1520 Spruce St.

1895. Ring, G. Oram, A.M., M.D., Ophthalmic Surgeon to the Episcopal Hospital; Ophthalmologist to the Widener Memorial Home for Crippled Children; Consulting Ophthalmologist to the American Oncologic Hospital. N. E. Cor. Seventeenth and Walnut Sts.

1899. Roberts, Walter, M.D., Professor of Otology in the Philadelphia Polyclinic; Otologist to the Methodist Episcopal Hospital; Laryngologist to the Philadelphia General Hospital. 1732 Spruce St.

1903. Robertson, William Egbert, M.D., Professor of Theory and Practice of Medicine and of Clinical Medicine in

ELECTED

Temple University; Physician to the Episcopal, Samaritan and Garretson Hospitals. 327 S. Seventeenth St.

1903. Robinson, William Duffield, Ph.G., M.D. 2012 Mount Vernon St.

1912. Rodman, John Stewart, M.D., Professor of Surgery, Woman's Medical College; Surgeon-in Chief, Woman's College Hospital; Attending Surgeon, Bryn Mawr Hospital; Assistant Surgeon to the Presbyterian Hospital. 1310 Medical Arts Building.

1909. Rosenberger, Randle C., M.D., Professor of Preventive Medicine and Bacteriology in the Jefferson Medical College. 2330 N. Thirteenth St.

*1907. Royer, B. Franklin, M.D. 370 Seventh Ave., New York City.

†1905. Rugh, James Torrance, A.B., M.D., Clinical Professor of Orthopædic Surgery in the Woman's Medical College of Pennsylvania; Orthopædic Surgeon to the Jefferson Medical College; Orthopædic Surgeon to the Methodist and the Philadelphia General Hospitals. 1616 Spruce St.

1897. Sailer, Joseph, Ph.B., M.D., Professor of Clinical Medicine in University of Pennsylvania; Physician to the Philadelphia General, the University, and Presbyterian Hospitals. 250 S. Eighteenth St.

1900. Sajous, Charles E. de M., M.D., LL.D., Sc.D., Officer of the Legion of Honor of France and of the Order of Leopold of Belgium; Professor of Endocrinology, Graduate School of Medicine, University of Pennsylvania; Emeritus Professor of Therapeutics in Temple University Medical School. 2043 Walnut St.

1905. Sartain, Paul J., A.M., M.D. 2006 Walnut St.

1908. Sautter, Albert C., M.D., Assistant in the Dispensary for Diseases of the Eye in the University Hospital; Assistant in the Eye Dispensary of the Lankenau Hospital. 1421 Locust St.

1906. Saylor, Edwin S., M.D., Chief Ophthalmologist to the Diagnostic Hospital of Philadelphia. 2100 Chestnut St.

1920. Scarlett, Hunter W., M.D. 230 S. Twenty-first St.

‡1910. Scarlett, Rufus B., M.D., Laryngologist to the Home for Consumptives at Chestnut Hill; Assistant in the Department for Diseases of the Ear, Throat, and Nose of the Pennsylvania Hospital; Instructor in Diseases of the Nose and Throat in the Philadelphia Polyclinic and College for Graduates in Medicine. 78 N. Clinton Ave., Trenton, N. J.

ELECTED

1917. SCHAEFFER, JACOB PARSONS, A.M., M.D., Ph.D., Professor of General Anatomy and Director of the Daniel Baugh Institute of Anatomy of the Jefferson Medical College. 4634 Spruce St.

1899. SCHAMBERG, JAY F., M.D., Professor of Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania; Director, Research Institute of Cutaneous Medicine. 1402 Spruce St.

1917. SCHNABEL, TRUMAN GROSS, A.B. (Lehigh), M.D., Associate in Medicine, University of Pennsylvania; Assistant Physician, Philadelphia General Hospital; Physician in the Medical Out-patient Department, University Hospital. 1704 Pine Street.

1917. SCHOFF, CHARLES H., M.D. Media, Pa.

1921. SCHUMANN, EDWARD ARMIN, A.B., M.D., Obstetrician and Gynecologist, Philadelphia General Hospital; Gynecologist, Frankford Hospital; Lecturer on Obstetrics, Jefferson Medical College; Consulting Gynecologist, Rush Hospital. 1814 Spruce St.

1887. DE SCHWEINITZ, GEORGE EDMUND, A.M., M.D., LL.D., Professor of Ophthalmology in the University of Pennsylvania; Consulting Ophthalmic Surgeon to the Orthopædic Hospital and Infirmary for Nervous Diseases, The Philadelphia Polyclinic and School for Graduates in Medicine, and the Philadelphia General Hospital; Ophthalmic Surgeon to the University Hospital. 1705 Walnut St.

*1913. DE SCHWEINITZ, GEORGE LORD, B.S., M.D., Assistant in the Department of Ophthalmology, St. Luke's Hospital, Bethlehem, Pa. 85 East Broad St., Bethlehem, Pa.

1910. SCHWENK, PETER N. K., M.A., M.D., Attending Surgeon to the Eye Department of the Pennsylvania Hospital; Attending Surgeon to the Wills Hospital. 1417 N. Broad Street.

1917. SERVICE, CHARLES A., M.D. Bala, Pa.

1924. SHALLOW, THOMAS A., M.D. 3942 Chestnut St.

1908. SHANNON, CHARLES E. G., A.B., M.D., Instructor in Ophthalmology in the Jefferson Medical College; Assistant in the Ophthalmological Clinic at the Jefferson Medical College Hospital; Ophthalmologist to the Seybert Institution. N. E. Corner Seventeenth and Walnut Sts.

1897. SHARPLESS, WILLIAM T., M.D., Physician to the Chester County Hospital. West Chester, Pa.

ELECTED

1906. SHIELDS, WILLIAM G., M.D., Dermatologist to Germantown Hospital; Chief of Dermatological Clinic and Assistant Physician to the Jewish Hospital. 414 School Lane, Germantown.

*1908. SHOEMAKER, HARLAN, A.B., M.D., Lecturer in Surgery, University of Southern California; Surgeon to Los Angeles County Hospital; Surgeon to Washington Street Clinic. 521 Bank of Italy Building, Los Angeles, Calif.

†1893. SHOEMAKER, HARVEY, M.D., Visiting Physician to the Sheltering Arms; Consulting Physician to the Southern Home for Destitute Children; Assistant Physician to the Lankenau Hospital; Physician to the Out-patient Department of the Lankenau Hospital. 1727 Spruce St.

†1896. SHOEMAKER, WILLIAM T., M.D., Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Clinical Professor of Ophthalmology in the Woman's Medical College of Pennsylvania; Ophthalmic Surgeon to Lankenau, Germantown and Pennsylvania Hospitals. 109 S. Twentieth St.

1900. SHUMWAY, EDWARD ADAMS, B.S., M.D., Ophthalmic Surgeon to the Philadelphia General, Lankenau and Children's Hospitals; Assistant Professor of Ophthalmology in the University of Pennsylvania, and Assistant Ophthalmic Surgeon to the University Hospital. 1737 Chestnut St.

1903. SINCLAIR, JOHN FALCONER, M.D., Epidemiologist, Presbyterian Hospital; Physician to the Philadelphia Orphan Asylum and to the Presbyterian Orphanage; Physician to the Home of the Merciful Saviour for Crippled Children. 4103 Walnut St.

1907. SINKLER, FRANCIS WHARTON, A.B., M.D., Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases. 1226 Medical Arts Bldg.

1902. SITER, E. HOLLINGSWORTH, M.D., Genito-urinary Surgeon to the Philadelphia General Hospital. 2213 DeLancey St.

1904. SKILLERN, PENN-GASKELL, M.D. 1633 Locust St.

1920. SKILLERN, ROSS HALL, M.D., Sc.D., Professor of Laryngology, Graduate School of Medicine, University of Pennsylvania; Laryngologist to Medico-Chirurgical Hospital. 1928 Chestnut St.

1904. SMITH, ALLEN J., A.M., M.D., Sc.D. (Penna. Coll.), LL.D. (McGill Univ.), Professor of Pathology and of Comparative Pathology and Director of Courses in Tropical Medicine in the University of Pennsylvania. Medical Laboratories, University of Pennsylvania.

ELECTED

1905. SMITH, S. MACCUEN, M.D., Professor of Otology in the Jefferson Medical College; Aurist and Laryngologist to the Germantown Hospital; Aurist to the Jewish Hospital; Consulting Aurist to the Memorial Hospital, Roxborough, and to the Oncologic Hospital. 1429 Spruce St.

1919. SMYTH, HENRY FIELD, M.D. Wayne, Pa.

1908. SPEESE, JOHN, M.D., Assistant Professor, Surgical Pathology, University of Pennsylvania; Associate Professor in Surgery, Graduate School of Medicine, University of Pennsylvania; Surgeon to the Children's and Presbyterian Hospitals. 1832 Spruce St.

1895. SPELLISSY, JOSEPH M., A.M., M.D., Visiting Surgeon to St. Joseph's and to the Methodist Episcopal Hospitals; Assistant Surgeon to the Orthopedic Department of the University Hospital. 317 S. Fifteenth St.

1897. SPILLER, WILLIAM G., M.D., Professor of Neurology in the University of Pennsylvania; Neurologist to the Philadelphia General Hospital. 4409 Pine St.

1894. STAHL, B. FRANKLIN, B.S., Ph.G., M.D., Visiting Physician to St. Agnes' and the Philadelphia General Hospitals. Haverford, Pa.

1909. STARBUCK, J. CLINTON, M.D., Physician to the Orphanage, Orphan Society of Philadelphia at Wallingford and to the Glen Mills School, Glen Mills, Pa. 42 E. Washington St., Media, Pa.

‡1875. STARR, LOUIS, M.D., LL.D. (Haverford). Care of Brown, Shipley & Co., London, England.

1912. STAUFFER, NATHAN PENNYPACKER, D.D.S., M.D., Laryngologist and Otologist to the Presbyterian Hospital; to the Philadelphia General Hospital, Tubercular Department; to the Home for Crippled Children. 2015 Walnut St.

1910. STELLWAGEN, THOMAS C., JR., M.D., Chief Clinical Assistant in the Out-patient Surgical Department of the Jefferson Medical College Hospital. 1912 Pine St.

1895. STENGEL, ALFRED, M.D., Sc.D., Professor of Medicine in the University of Pennsylvania; Physician to the University Hospital and the Pennsylvania Hospital. 1728 Spruce St.

1901. STEVENS, ARTHUR A., M.D., Professor of Materia Medica, Therapeutics and Clinical Medicine in the Woman's Medical College of Pennsylvania; Lecturer on Physical Diagnosis in the University of Pennsylvania; Physician to the Episcopal and St. Agnes' Hospitals. 314 S. Sixteenth Street.

ELECTED

1914. Stewart, Thomas S., B.S. (Univ. of Penna.), M.D. 1532 Pine St.

1925. Stokes, John H., A.B., M.D., Professor of Dermatology and Syphilology, School of Medicine, University of Pennsylvania; Professor of Dermatology, Graduate School of Medicine, University of Pennsylvania; Attending Dermatologist, University and Philadelphia General Hospitals; Dermatologist, Medico-Chirurgical and Polyclinic Hospitals. 3800 Chestnut St.

1921. Stoner, William H., A.M., Ph.C., Pharm. D., M.D., Associate Professor of Biochemistry and Diseases of Metabolism, Graduate School of Medicine, University of Pennsylvania; Assistant Metabolic Physician, Philadelphia General Hospital. Medical Laboratories, University of Pennsylvania.

1898. Stout, George C., M.D., Consulting Laryngologist and Aurist to the Presbyterian Hospital, the Children's Aid Society and the William Penn Charter School. 2015 Walnut St.

1923. Strecker, Edward, A., A.M., M.D., Medical Director of Department for Mental and Nervous Diseases and Neurologist to Pennsylvania Hospital and Chief of the Out-patient Neuro-psychiatric Clinic; Neurologist, Misericordia Hospital; Assistant Professor of Psychiatry, Graduate School of Medicine, University of Pennsylvania. 4401 Market St.

1923. Stroud, William D., M.D. 1011 Clinton St.

1923. Strouse, Frederick M., M.D. 1301 Spruce St.

1884. Stryker, Samuel S., M.D., Consulting Physician to the Presbyterian Hospital. 3833 Walnut St.

*1900. Swan, John M., M.D., Attending Physician, Park Avenue Clinical Hospital. 457 Park Avenue, Rochester, New York.

1898. Sweet, William M., M.D., Professor of Ophthalmology in the Jefferson Medical College, and Ophthalmic Surgeon to the Jefferson Medical College Hospital; Consulting Surgeon to the Wills Hospital. 1205 Spruce Street.

1900. Talley, James Ely, A.B., M.D., Professor of Cardiology, Graduate School of Medicine, University of Pennsylvania; Physician to the Presbyterian and Methodist Episcopal Hospitals. 1811 Spruce St.

1886. Taylor, John Madison, A.B. and A.M. (Princeton), M.D., Professor of Physical Therapeutics and Dietetics, Medical Department Temple University. 1504 Pine St.

ELECTED

1887. TAYLOR, WILLIAM J., M.D., Surgeon to the Orthopædic Hospital and Infirmary for Nervous Diseases, and to St. Agnes' Hospital; Consulting Surgeon to the West Philadelphia Hospital for Women. 1825 Pine St.

1886. TAYLOR, WILLIAM L., M.D. 2223 Tioga St.

†1910. THOMAS, BENJAMIN A., A.B., A.M., M.D., Vice-Dean and Professor of Urology, Graduate School of Medicine, University of Pennsylvania; Genito-urinary Surgeon, Presbyterian Hospital; Consulting Genito-urinary Surgeon, Pennsylvania Railroad and to the Prison, Philadelphia. 116 S. Nineteenth St.

1912. THOMAS, FRANK WISTER, A.M., M.D., Visiting Physician to "Buttercup Cottage;" Consulting Physician to the Germantown Hospital. 27 E. Mt. Airy Ave.

1907. THOMAS, THOMAS TURNER, M.D., Associate Professor of Applied Anatomy and Associate in Surgery in the University of Pennsylvania; Surgeon to the Philadelphia General Hospital; Assistant Surgeon to the University Hospital. 2009 Spruce St.

1896. THORINGTON, JAMES, A.M., M.D., Consulting Ophthalmic Surgeon to the Presbyterian Hospital; Ophthalmologist to the Ellwyn, Pa., Training School for Feeble-minded Children. 2031 Chestnut St.

1898. THORNTON, EDWARD Q., M.D., Assistant Professor of Materia Medica in the Jefferson Medical College. 1331 Pine St.

1912. TORREY, ROBERT G., M.D., Physician to the Philadelphia General Hospital; Associate in Medicine, University of Pennsylvania. 1716 Locust St.

1896. TOULMIN, HARRY, M.D., Vice-President, Medical Department, Penn Mutual Life Insurance Company. Haverford, Pa.

1908. TRACY, STEPHEN E., M.D., Gynecologist to the Stetson Hospital; Visiting Surgeon to the Gynecean Hospital. 1527 Spruce St.

*1901. TUCKER, HENRY, M.D. Bellevue, Md.

†1894. TUNIS, JOSEPH PRICE, M.D., Assistant Professor of Histology and Embryology, Temple University. Chestnut Hill, Philadelphia.

1924. TURNER, CHARLES ROOT, A.B., D.D.S., M.D., Dean, School of Dentistry, University of Pennsylvania. Merion, Pa.

1923. TURNER, CREIGHTON H., M.D., Associate in Medicine, Jefferson Medical College; Visiting Physician, St. Agnes' Hospital. 1731 Pine St.

ELECTED

‡1901. TURNER, JOHN B., M.D., Ph.D., Assistant in the Ophthalmological Clinic, Methodist Episcopal Hospital. 1833 Chestnut St.

1897. TYSON, T. MELLOR, M.D., Physician to the Philadelphia General Hospital; Physician to the Rush Hospital, the Philadelphia Lying-in-Charity Hospital and the Children's Aid Society of Philadelphia. 1506 Spruce St.

1907. ULLOM, JOSEPHUS TUCKER, M.A., M.D., Physician to the Chestnut Hill Hospital. Carpenter and Quincy Streets, Germantown.

*1913. VAIL, WILLIAM PENN, B.S., M.S., M.D., Laryngologist to the Pennsylvania Institution for the Instruction of the Blind; Laryngologist to the Department for Tuberculosis of the Philadelphia General Hospital; Assistant Laryngologist and Otologist to the Out-patient Department of the Pennsylvania Hospital; Assistant Laryngologist to the Children's Hospital. Blairstown, N. J.

°1873. VAN HARLINGEN, ARTHUR, Ph.B. (Yale), M.D., Emeritus Professor of Diseases of the Skin in the Philadelphia Polyclinic. 1831 Chestnut St.

1903. VAN PELT, WILLIAM TURNER, M.D. Chestnut Hill, Philadelphia.

1893. VANSANT, EUGENE LARUE, M.D. 2046 Chestnut St.

1912. VAUX, NORRIS WISTAR, M.D., Surgeon to the Chestnut Hill Hospital; Surgeon to the Dispensary of the Germantown Hospital. 1810 S. Rittenhouse Square.

*1897. VEASEY, CLARENCE A., A.M., M.D. Suite 404, Paulsen Building, Spokane, Wash.

†1883. VINTON, CHARLES HARROD, A.M., M.D. P. O. Box 464, Atlantic City, N. J.

1903. WADSWORTH, WILLIAM SCOTT, M.D. 3914 Baltimore Ave.

1906. WALKER, JOHN K., M.D., Physician to the Children's Hospital of the Mary J. Drexel Home; Physician to the Out-patient Department of the Pennsylvania Hospital. 1814 Pine St.

1907. WALKER, WARREN, M.D., Dermatologist to the Episcopal and Bryn Mawr Hospitals. 1819 Chestnut St.

1904. WALSH, JOSEPH, A.M., M.D., Visiting Physician to and Medical Director of the White Haven Sanatorium. Medical Arts Building.

ELECTED

1910. Ward, E. Tillson, A.M., M.D. 2006 Mt. Vernon St.

1895. Watson, Arthur W., M.D., Professor of Diseases of the Throat and Nose in the Philadelphia Polyclinic and College for Graduates in Medicine; Laryngologist to the Jewish Hospital; Laryngologist and Aurist to the Mt. Sinai Hospital; Laryngologist to Home for Incurables. 2013 Locust St.

‡1886. Watson, Edward W., M.D., Physician to the Magdalene Home. 38 S. Nineteenth St.

1923. Watson, William R., M.D., Chief Laryngologist, Episcopal and Diagnostic Hospitals; Assistant Chief Laryngologist, Pennsylvania Hospital. 2124 Pine St.

1903. Weber, Charles H., M.D., Associate in Pediatrics, Graduate School of Medicine, University of Pennsylvania; Physician to the Medical Dispensary, Children's Hospital; Pediatrist, Howard Hospital and to the Municipal Court. 1811 Spruce Street.

1920. Weidman, Fred. D., M.D., Professor of Dermatological Research, University of Pennsylvania; Assistant Pathologist, Philadelphia Zoölogical Garden; Attending Dermatologist, Philadelphia General Hospital. 20 Tenby Road, Llanerch, Pa.

1906. Weisenburg, Theodore H., M.D., Professor of Neuro-Psychiatry, Graduate School of Medicine, University of Pennsylvania; Neurologist, Philadelphia General Hospital and Physician to Orthopædic Hospital and Infirmary for Nervous Diseases. 2037 DeLancey St.

1923. Weiss, Edward, M.D., Demonstrator of Clinical Medicine, Jefferson Medical College; Assistant Attending Physician, Jewish Hospital and in the Tuberculosis Wards, Philadelphia General Hospital. 1906 Walnut St.

1913. Wells, P. Frailey, A.M., M.D., Ph.D., 754 N. Fortieth St.

1893. Westcott, Thompson S., M.D., Associate in Diseases of Children in the University of Pennsylvania; Pediatrist to the Methodist Episcopal Hospital; Consulting Physician, Haddock Memorial Home. 1720 Pine St.

‡1884. Wharton, Henry R., M.D., Consulting Surgeon to the Presbyterian and the Children's Hospitals; Surgeon to Girard College; Consulting Surgeon to the Bryn Mawr Hospital, the Chestnut Hill Hospital, St. Christopher's Hospital for Children, the Pennsylvania Institution for the Deaf and Dumb, and the Pennsylvania Institution for the Blind. Berwyn, Pa.

ELECTED

1921. WHITAKER, WILLIAM, M.D., Surgeon to Dispensary of the Episcopal Hospital. 5448 Germantown Ave.

1901. WHITE, COURTLAND Y., M.D., Director of the Pathological Laboratories of the Episcopal Hospital; Pathologist to the Children's Hospital and to the Kensington Hospital for Women; Chief Bacteriologist to the Bureau of Health, Department of Health and Charities, Philadelphia. 6611 N. Tenth St.

*1905. WHITEWAY, HAROLD M., M.D. 2356 W. Twenty-first St., Los Angeles, Calif.

1898. WHITING, ALBERT D., M.D., Associate Professor of Surgery, Graduate School of Medicine, University of Pennsylvania; Associate Surgeon, Lankenau Hospital; Surgeon, Germantown Hospital. 333 S. Eighteenth St.

1925. WIDMANN, BERNARD P., M.D., 1321 Spruce St.

1914. WILLARD, DE FOREST P., B.S. (Univ. of Penna.), M.D., Professor of Orthopædics, Graduate School of Medicine, University of Pennsylvania; Orthopædic Surgeon to the Polyclinic, Jewish and Delaware Hospitals. 1630 Spruce St.

1907. WILLIAMS, CARL, B.S., M.D., Ophthalmic Surgeon to the Germantown Hospital; Instructor in Ophthalmology in the University of Pennsylvania; Ophthalmic Surgeon to the Pennsylvania Institution for the Deaf and Dumb. School Lane and Greene Sts., Germantown.

1924. WILLIAMS, HORACE JAMES, M.D. 5908 Greene St. Germantown.

1920. WILLIAMS, PHILIP F., Ph.B., M.D., Assistant Professor of Obstetrics, Graduate School of Medicine, University of Pennsylvania; Instructor in Obstetrics, School of Medicine, University of Pennsylvania; Obstetrician to the Maternity Hospital of Philadelphia and Assistant Gynecologist to the Presbyterian Hospital. 2206 Locust St.

1916. WILMER, HARRY B., M.D., Assistant Instructor in Medicine, University of Pennsylvania; Assistant Visiting Physician and Assistant Neurologist to the Germantown Hospital; Visiting Chief to the Dispensary of the Germantown Hospital. 138 W. Walnut Lane, Germantown.

1921. WILSON, GEORGE, M.D., Instructor in Medicine and Neurology, School of Medicine, University of Pennsylvania; Assistant Physician, Philadelphia Hospital; Assistant Neurologist, Philadelphia, University and Children's Hospitals; Consulting Neurologist, St. Christopher's Hospital and the Pennsylvania Training School for Feeble-minded Children. N. E. Cor. Twentieth and Chestnut Sts.

ELECTED

1874. Wilson, James Cornelius, A.M. (Princeton), M.D., Emeritus Professor of the Practice of Medicine and of Clinical Medicine in the Jefferson Medical College; Physician-in-Chief to the Lankenau Hospital; Emeritus Physician to the Pennsylvania Hospital; Consulting Physician to the Bryn Mawr Hospital. 1509 Walnut St.

1902. Wilson, Samuel M., M.D. 2018 Chestnut St.

1897. Wilson, W. Reynolds, M.D. Villa Nova, Pa.

1904. Wister, James W., M.D., Physician to the Out-patient Department of the Germantown Hospital. 5430 Germantown Ave.

*1901. Witmer, A. Ferree, M.D. 21 North Grand Ave., Baldwin, N. Y.

1918. Wolferth, Charles Christian, A.B., M.D., Associate in Medicine, University of Pennsylvania; Associate in Cardiac Pathology, William Pepper Laboratory of Clinical Medicine, University of Pennsylvania. 1704 Pine St.

1893. Wood, Alfred C., M.D., Assistant Professor of Surgery in the University of Pennsylvania; Surgeon to the University, the Philadelphia General, St. Timothy's and the Howard Hospitals. 2035 Walnut St.

1900. Wood, George, B., M.D., Laryngologist and Otologist, Orthopædic and Howard Hospitals; Professor of Laryngology, Graduate School, University of Pennsylvania. N. E. Cor. Twentieth and Chestnut Sts.

1903. Wood, Horatio C., Jr., M.D., Professor of Pharmacology and Therapeutics in the University of Pennsylvania; Professor of Materia Medica, Philadelphia College of Pharmacy and Science. 319 S. Forty-first St.

°1880. Woodbury, Frank, M.D., Secretary to the Committee on Lunacy of the Board of Charities of Pennsylvania. 101 Allen Lane, Mt. Airy.

*1911. Woods, Andrew H., A.B., M.D., Professor and Head of the Neurological Department, Peking Union Medical College, Peking, China.

†1897. Woodward, George, M.D. W. Willow Grove Ave., Chestnut Hill, Philadelphia.

1903. Worden, Charles B., A.M., M.D. Princeton, N. J.

1894. Zentmayer, William, M.D., Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania; Attending Surgeon to the Wills Hospital; Ophthalmologist to the Glen Mills School. 1506 Spruce St.

ELECTED

1899. Ziegler, S. Lewis, A.M., M.D., LL.D., Attending Surgeon to the Wills Hospital; Chief Ophthalmic Surgeon to St. Joseph's Hospital; Membre Société Française d'Ophthalmologie. 1625 Walnut St.

1887. Ziegler, Walter M. L., A.M., M.D. 1418 N. Seventeenth St.

1895. Zimmerman, Mason W., M.D., Consulting Ophthalmic Surgeon to the Germantown Hospital. 1518 Waverly St.

# ASSOCIATE FELLOWS

(Limited to Fifty, of whom Twenty may be Foreigners)

## American

ELECTED

1911. Abbe, Robert, M.D. 40 W. Fifty-ninth St., New York City, New York.

1909. Billings, Frank, M.D., 1550 North State Parkway, Chicago, Illinois.

1880. Carrow, Flemming, M.D., 823 David Whitney Building, Detroit, Mich.

1893. Councilman, William T., M.D., Harvard Medical College, Boston, Massachusetts.

1909. Crile, George W., M.D., 1021 Prospect Avenue, S. E., Cleveland, Ohio.

1909. Dana, Charles Loomis, M.D., 53 West Fifty-third Street, New York City, New York.

1892. Emmet, Thomas Addis, M.D., 91 Madison Avenue, New York City, New York.

1916. Estes, William Lawrence, M.D., South Bethlehem, Pa.

1912. McCaw, Brig.-Gen. Walter D., M.D. Assistant Surgeon-General, U. S. A., Army Medical School, Washington, D. C.

1906. Mayo, William J., M.D., Rochester, Minnesota.

1917. Miner, Charles H., M.D., Wilkes-Barre, Pa.

1906. Pilcher, Lewis Stephen, M.D., 145 Gates Avenue, Brooklyn, New York.

1906. Shattuck, Frederick C., M.D., 135 Marlborough Street, Boston, Massachusetts.

1894. Warren, J. Collins, M.D., 58 Beacon Street, Boston, Massachusetts.

1894. Weir, Robert F., M.D., 16 East Ninety-sixth St., New York City, New York.

1892. Welch, William H., M.D., Johns Hopkins Hospital, Baltimore, Maryland.

## Foreign

1890. Baccelli, Guido, Rome, Italy.
1908. Bannerman, W. B., M.D., General, I. M. S., 11 Strathearn Place, Edinburgh, Scotland.
*1916. Guitéras, John, M.D., Benavides, Cuba.
1924. Hopkins, F. Gowland, M.D., Cambridge, England.
1909. Macallum, Archibald B., M.A., M.B., Ph.D., Sc.D., LL.D., F.R.S., Department of Biochemistry, McGill University, Montreal, Canada.
1922. McCarrison, Lieut.-Col., Robert, M.D. (London), D.Sc. (Oxford, Eng.), LL.D., C.I.E., Deficiency Diseases, Pasteur Institute of Southern India. Coonoor, S. India.
1924. Macleod, John James R., M.D., Toronto, Canada.
1906. Myles, Sir Thomas, M.D., 33 Merion Square, W., Dublin, Ireland.
1885. Rendu, Jean, M.D., Lyons, France.
1908. Ross, Col. Sir Ronald, K.C.B., K.C.M.G., F.R.S., M.D., D.Sc., LL.D., 36 Harley House, London, N. W. I., England.

* Deceased.

# NECROLOGICAL LIST

FELLOWS

| | |
|---|---|
| CHARLES B. PENROSE, M.D. | February 27, 1925 |
| JOHN B. TURNER, M.D. | March 3, 1925 |
| I. MINIS HAYS, M.D. | June 5, 1925 |
| RUFUS B. SCARLETT, M.D. | July 11, 1925 |
| LOUIS STARR, M.D. | September 12, 1925 |
| JOHN C. HIRST, M.D. | October 4, 1925 |
| LOUIS JURIST, M.D. | October 9, 1925 |
| JOHN H. W. RHEIN, M.D. | October 14, 1925 |
| JOHN GUITERAS, M.D. | October 28, 1925 |
| RICHARD H. HARTE, M.D. | November 14, 1925 |
| EDWARD W. WATSON, M.D. | November 20, 1925 |
| HENRY R. WHARTON, M.D. | December 3, 1925 |

# LIST OF PRIZES AND LECTURES

## THE WILLIAM F. JENKS MEMORIAL PRIZE

(Triennial)

| | | |
|---|---|---|
| 1889 | John Strahan, M.D. | Belfast (Ireland). |
| 1895 | Abram Brothers, M.D. | New York. |

NOTE—June 12, 1900, the William F. Jenks Memorial Prize Fund was transferred to the Library as the "William F. Jenks Memorial Library Fund."

## ALVARENGA PRIZE OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA

(Annual)

| | | |
|---|---|---|
| 1890 | R. W. Philip, M.D. | Edinburgh (Scotland). |
| 1891 | L. Duncan Bulkley, M.D. | New York. |
| 1892 | R. H. L. Bibb, M.D. | Saltillo. |
| 1894 | G. E. de Schweinitz, M.D. | Philadelphia. |
| 1895 | Guy Hinsdale, M.D. | Philadelphia. |
| 1897 | Joseph Collins, M.D. | New York. |
| 1898 | S. A. Knopf, M.D. | New York. |
| 1898 | Robert Randolph, M.D. | Baltimore. |
| 1900 | David de Beck, M.D. | Cincinnati. |
| 1901 | George W. Crile, M.D. | Cleveland. |
| 1903 | William S. Carter, M.D. | Galveston. |
| 1905 | D. Chalmers Watson, M.D. | Edinburgh (Scotland). |
| 1907 | William Louis Chapman, M.D. | Providence. |
| 1908 | William T. Shoemaker, M.D. | Philadelphia. |
| 1910 | M. Katzenstein, M.D. | Berlin (Germany). |
| 1911 | Francis D. Patterson, M.D. | Philadelphia. |
| 1914 | H. B. Sheffield, M.D. | New York. |
| 1915 | J. E. Sweet, M.D. | Philadelphia. |
| 1917 | Wilburt C. Davison, M.D. | Baltimore. |
| 1921 | John W. Churchman, M.D. | New York. |
| 1923 | Edward P. Heller, M.D. | Kansas City, Mo. |
| 1924 | Gordon Cameron, M.B., B.S. | Victoria, Australia. |
| 1925 | Raphael Isaacs, M.D. | Boston. |

## NATHAN LEWIS HATFIELD PRIZE FOR ORIGINAL RESEARCH IN MEDICINE

(Triennial)

| | | |
|---|---|---|
| 1901 | Henry F. Harris, M.D. | Atlanta. |
| 1909 | Martin Henry Fischer, M.D. | Oakland. |
| 1917 | A. B. Macallum, M.D., F.R.S. | Toronto. |
| 1919 | Harvey Cushing, M.D. | Boston. |
| 1921 | William R. Nicholson, M.D. | Philadelphia. |
| 1922 | Sir Thomas Lewis, C.B.E., M.D., F.R.S. | London (Eng.). |
| 1923 | Frederick Grant Banting, M.D., | Toronto. |
| 1924 | George J. Heuer, M.D. | Cincinnati. |

NOTE.—November 29, 1913, by Supplemental Deed of Trust, the title of this Fund was changed to "Nathan Lewis Hatfield Prize and Lectureship."

## WEIR MITCHELL LECTURES

| | | |
|---|---|---|
| Jan. 17, 1911 | Arthur R. Cushny, M.D. | London. |
| Mar. 30, 1911 | Edmund B. Wilson, Ph.D., LL.D. | New York. |
| May 16, 1911 | Svante Arrhenius | Stockholm. |
| Nov. 3, 1911 | William T. Porter, M.D. | Boston. |
| Mar. 29, 1912 | William H. Howell, M.D. | Baltimore. |
| Oct. 21, 1912 | G. H. F. Nuttall, F.R.S., M.D. | Cambridge (Eng.). |
| April 4, 1913 | H. P. Armsby, Ph.D., LL.D. | Pennsylvania. |
| Feb. 25, 1914 | Harvey Cushing, M.D. | Boston. |

## PUBLIC LECTURES

| | | |
|---|---|---|
| Feb. 16, 1910 | S. Weir Mitchell, M.D. | Philadelphia. |
| Nov. 17, 1910 | Simon Flexner, M.D. | New York. |
| Dec. 15, 1910 | William H. Welch, M.D. | Baltimore. |
| April 18, 1911 | James G. Mumford, M.D. | Clifton Springs, N.Y. |
| Nov. 20, 1911 | Talcott Williams, A.M., LL.D., Litt.D. | Philadelphia. |
| April 29, 1912 | Owen Wister, A.M., LL.D. | Philadelphia. |
| Feb. 17, 1913 | John K. Mitchell, M.D. | Philadelphia. |
| Feb. 15, 1916 | Daniel J. McCarthy, M.D. and Walter Estell Lee, M.D. | Philadelphia. |
| April 15, 1916 | Surgeon A. M. Fauntleroy | U. S. Navy. |

## MARY SCOTT NEWBOLD LECTURES

| | | |
|---|---|---|
| Mar. 29, 1917 | A. T. McCormack, M.D. | Bowling Green, Ky. |
| April 4, 1919 | Col. Thomas W. Salmon, M.C., | U. S. Army. |
| Feb. 6, 1920 | Alonzo E. Taylor, M.D. | Philadelphia. |
| Feb. 4, 1921 | Maj.-Gen. Merritte W. Ireland | Washington. |
| April 20, 1921 | Prof. William Romaine Newbold, | Philadelphia. |
| Nov. 11, 1921 | Robert McCarrison, M.D., D.Sc., LL.D. | Oxford (Eng.). |
| Feb. 1, 1922 | Hans Zinsser, M.D. | New York. |
| April 5, 1922 | G. Canby Robinson, M.D. | Baltimore. |
| Dec. 6, 1922 | Donald C. Balfour, M.D. | Rochester, Minn. |
| Mar. 7, 1923 | J. J. R. Macleod, M.D. | Toronto. |
| April 4, 1923 | Prof. Leon Asher, M.D. | Berne (Switzerl'd). |
| Mar. 5, 1924 | Prof. A Biedl | Prague (Czecho-Slovakia). |
| April 15, 1924 | J. G. FitzGerald, M.D. | Toronto. |
| Oct. 31, 1924 | John I. Hunter, M.D., and N. D. Royle, M.D. | Sydney (Australia). |
| Dec. 4, 1924 | Willem Einthoven, M.D. | Leyden (Holland). |
| April 21, 1925 | A. N. Richards, A.M., Ph.D. | Philadelphia. |

## MÜTTER LECTURES

| | | |
|---|---|---|
| 1865 | J. H. Packard, M.D. | Philadelphia. |
| 1866 | J. H. Packard, M.D. | Philadelphia. |
| 1867 | J. H. Packard, M.D. | Philadelphia. |
| 1868 | Harrison Allen, M.D. | Philadelphia. |
| 1869 | J. H. Brinton, M.D. | Philadelphia. |
| 1872 | J. da S. Solis Cohen, M.D. | Philadelphia. |
| 1879 | S. W. Gross, M.D. | Philadelphia. |
| 1882 | E. O. Shakespeare, M.D. | Philadelphia. |
| 1885 | H. F. Formad, M.D. | Philadelphia. |
| 1888 | O. H. Allis, M.D. | Philadelphia. |
| 1890–1891 | Roswell Park, M.D. | Buffalo. |
| 1893–1894 | De Forrest Willard, M.D., and Guy Hinsdale, M.D. | Philadelphia. |
| 1896 | O. H. Allis, M.D. | Philadelphia. |
| 1899–1900 | J. B. Roberts, M.D. | Philadelphia. |
| 1901 | H. W. Cushing, M. D. | Boston. |
| 1902 | L. A. La Garde, M.D. | Washington. |
| 1903 | C. N. B. Camac, M.D. | New York. |
| 1904 | G. H. Monks, M.D. | Boston. |
| 1905 | A. O. J. Kelly, M.D. | Philadelphia. |

| | | |
|---|---|---|
| 1906 | W. J. Mayo, M.D. | Rochester, Minn. |
| 1907 | J. Rogers, M.D., and S. P. Beebe, M.D. | New York. |
| 1908 | G. W. Crile, M.D. | Cleveland. |
| 1909 | H. D. Fry, M.D, | Washington. |
| 1910 | T. W. Hastings, M.D. | New York. |
| 1911 | C. F. Nassau, M.D. | Philadelphia. |
| 1912 | J. C. Bloodgood, M.D. | Baltimore. |
| 1913 | R. C. Coffey, M.D. | Portland, Ore. |
| 1914 | F. H. Albee, M.D. | New York. |
| 1915–1916 | Rudolph Matas, M.D. | New Orleans, La. |
| 1916 | Nelson M. Percy, M.D. | Chicago, Ill. |
| 1917 | Chevalier Jackson, M.D. | Philadelphia. |
| 1919 | Alexis V. Moschcowitz, M.D. | New York. |
| 1920 | J. Chalmers Da Costa, M.D. | Philadelphia. |
| 1921 | Prof. H. C. Jacobaeus | Stockholm (Swed.). |
| 1922 | James Ewing, M.D. | New York. |
| 1923 | J. Edwin Sweet, M.D. | Philadelphia. |
| 1924 | Evarts Graham, M.D. | St. Louis. |
| 1925 | Edward Archibald, M.D. | Montreal, Can. |

WEIR MITCHELL ORATION

| | | |
|---|---|---|
| 1919 | Charles W. Burr, M.D. | Philadelphia. |
| 1922 | Charles Loomis Dana, M.D. | New York. |
| 1925 | Simon Flexner, M.D. | New York. |

# MEMOIR OF CHARLES B. PENROSE, M.D.[1]

By EDWARD MARTIN, M.D.

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All men are born, and die. Most men marry. Many men fill, and worthily, public positions, are members of important commissions or boards, acquire wealth. These are matters of import during the life of the individual, or shortly thereafter, and to those with whom he has had social, professional or business relations. The data bearing on these matters are appended to this memorial.

As to the Penrose forbears, his brother, Richard A. F. Penrose, geologist of international reputation, president of the Academy of Natural Sciences, founder and one-time president of the Society of Economic Geologists, answered a query on this subject as follows: "On my father's side our first ancestor in this country was Bartholomew Penrose, who came to Philadelphia with William Penn about 1700. On our mother's side our direct ancestor was Governor Dudley of Massachusetts. Our ancestors on both sides have tried to be respectable, law-abiding people."

This brief answer could be abundantly supplemented by consulting a book in the library of the Pennsylvania Historical Society, entitled, *History of the Penrose Family of Philadelphia*. As is true of the present generation, each of its predecessors has rendered distinguished service to state and nation.

Many Penroses of note might have been mentioned by Richard Penrose. He answered in accordance with the broad general principle that undue pride in worthy ancestors is taken mainly by those who do not have them or, having them, have not met the obligation imposed thereby.

Charles B. Penrose was one of a family of long, strong, lean, handsome, active boys; guided in childhood by their exceptionally able, gifted and devoted mother; later by their cultured and distinguished

[1] Read October 7, 1925.

father, Dr. R. A. F. Penrose, professor of obstetrics in the University of Pennsylvania. To him, their father, because of his wordly wisdom, deep affection and abiding belief in them, they rendered respect and obedience. With him, because of his vivid interest, full understanding and large charity, they were as unrestrained in thought, word and action as with each other.

In the seventies of last century, on a gale-swept sea, there was but one boat, a small one, under double reef, quartering for the Atlantic City Inlet. A storm-bound yachtsman said to a captain of a boat-for-hire, "No human being should go out on a day like this. If he does he has no right to expect to get back." The captain of the boat-for-hire, replied: "They ain't humans, they're Penrose boys. They always get back."

Charles Penrose's first school was the Episcopal Academy; thence he went to Harvard, while a student contributing to scientific journals papers upon mathematical and physical subjects. He graduated with highest honors in physics in his nineteenth year. Such was his aptitude for this branch of science that, together with his A.B. degree, he was offered an assistant professorship, in the belief that he might become one of the leading physicists of his generation.

On leaving Harvard he entered the medical school of the University of Pennsylvania, at the same time continuing his studies in mathematics and physics at Harvard, where by special permission of the University Council, and on condition that he should spend two months of each yearly term at Harvard, he was allowed to try for the degree of Ph.D. In the spring of 1884, and at the age of twenty-two, he was given the degree of M.D. by the University of Pennsylvania and that of Ph.D. in physics by Harvard.

After completing his internship at the Pennsylvania Hospital, and while attached to its out-patient department and that of the old Philadelphia Dispensary, Penrose, operating in cellar and attic, convinced the profession that recovery from abdominal section could be made habitual rather than occasional; and that thereby many women condemned to a life of misery or a speedy death could be made well. It was about this time that the professor of surgery of the University of Pennsylvania characterized the abdominal operations of his colleague, the professor of gynecology, as "legalized murder"—and with some justice in so far as mortality was concerned.

It was while he was demonstrating, to a then skeptical profession, the safety of clean, deft, abdominal surgery, that as an outlet to his superabundant vitality, Penrose swam the thirteen miles from Philadelphia to Chester. Thereafter, though not necessarily incident thereto, he suffered from persistent cough with fever and loss of weight. Hoping that air, altitude, sunlight and exercise might cure him he went to Cheyenne and dug with a shovel daily, leaving a landmark to which strangers were taken for years. Dr. A. W. Barber, then governor of Wyoming, wrote at this time: "Penrose is past all help. I doubt if you ever see him again."

When the big cattlemen with their cowboys and killers rode through Cheyenne on their mission of rustler extermination, Penrose joined them as surgeon, but was taken so desperately ill that in spite of his protests he was sent back to the town of Douglas. He was jailed on sight, which saved him from being shot. Believing his bichlorid tablets were intended for poisoning the wells, lynching was promptly decided upon, but postponed until morning in the interest of a larger audience. His cellmate, red-handed murderer and horse-thief, offered him half of a pair of scissors, holding that suicide even by such a poor instrument was better than hanging. A special train from Cheyenne, sent by Governor Barber, carrying a United States marshal, robbed the mob of its anticipated pleasure, for which its appetite had been whetted by shooting through the cell window most of the night.

From Cheyenne he went to Silver City, New Mexico, where he made a rapid and complete recovery. Thereafter he married Miss Kathryn Drexel, of New York, and accepted the professorship of gynecology in the University of Pennsylvania. This department he organized and administered with his characteristic skill and thoroughness. His textbook on *Diseases of Women* was welcomed as a standard. He taught rational, clean, gentle surgery by word and hands in a way both convincing and proselytizing. He had the hero worship of his students, the confidence and respect of his colleagues, a large consulting and private practice and a leading place among the surgeons of America.

A recurrence of his lung trouble forced him to resign all this and to devote himself to its arrest or cure.

To meet the obvious and urgent need of a hospital for women, Penrose founded, organized, incorporated, and, through his friends financed the Gynecean Hospital (1887); having associated with him

at first Dr. Joseph Price, then Drs. D. Hayes Agnew and J. Montgomery Baldy; the latter most ably carrying for many years the surgical and executive burden of the institution.

During the late war and thereafter, Penrose and Baldy, in the larger interests of public health and because the need seemed urgent, devoted the hospital to the sequestration until rendered non-contagious, of venereally infected women sent by the Municipal Court. Room was made for sixty; a dispensary with an average attendance of one hundred was opened nightly for those not under court control. Threatened failure of the city to coöperate in more extensive plans having for their end the lessening of venereal incidence, led to the closing of the Gynecean Hospital in 1924. In accordance with Penrose's wish the interest from the Gynecean Estate of something short of a half million dollars has been devoted to research; now being conducted under the supervision of the gynecological department of the University of Pennsylvania.

Baldy writes: "Without the Penrose financial and other backing there never would have been such a hospital. Penrose was from the beginning to the day he died its moving power and prime supporter."

In 1903 he conceived and created the Pennsylvania Department of Health, giving to its commissioner extraordinary power. His conception was put in such impregnable legal phraseology by Mr. Eli K. Price that all attacks upon it have failed. Penrose saw personally every member of the legislature the night before the passage of his bill and named the first commissioner of health, Dr. Samuel G. Dixon. This might not have been possible except for the active support of his brother, Honorable Boies Penrose, then and until his death the dominant influence in both state and national politics.

In 1899, Penrose was appointed a member of the Game Commission of Pennsylvania, becoming its president in 1911. From the beginning of his service therein he was director of its policies.

Pennsylvania now has thirty-four game refuges, containing about 30,000 acres, surrounded by 1,200,000 acres of state forest, the latter available for hunting. Nearly 8000 deer, nearly 1000 bear, over a half million grouse, three to four million rabbits, several thousand turkeys, and other game birds and animals are annually shot by the nearly half-million licensed hunters of the state.

In 1922, being opposed to commission control, the governor of

Pennsylvania asked Mr. F. C. Walcott, who was known to hold similar views, to report on the Game Commission. Quoting in part from Walcott's report (on the authority of Dr. George Bird Grinnell, as corrected by Seth E. Gordon, May 5, 1925): "You perhaps know that I am opposed to the commission form of government in game matters. Usually none of the commissioners appointed take any active interest in the work. Pennsylvania is the exception which proves the rule. Personally, I think it would be a calamity if any other plan were adopted. The sportsmen are satisfied, and their present plan and policy have made Pennsylvania one of the greatest game states in the Union, from a state that was practically shot out when they took hold of it."

Dr. Grinnell writes: "For a matter of twenty years Penrose was the leading man on the commission. He devoted to it more time and energy than all the others put together. No legislation was passed and nothing was done that he did not approve. We all recognize the fact that in any great work of this sort no single man does it all, and to no single man should come the sole credit for the work, but there is always a leader, and in Pennsylvania that leader was Penrose."

From the beginning of his direction of the Zoölogical Garden, Penrose pursued the policy of making an exhibit unrivaled both in the variety of animals shown and in the maintenance of their health. He, with the assistance of Drs. William Pepper, M. T. Ravenel, C. Y. White, Leonard Pearson, and Herbert Fox, conducted autopsies from the findings of which the principles of preventive medicine were so applied that, among other betterments in animal health, tuberculosis in the monkey was practically abolished.

Penrose gave and raised funds for new construction and for remodeling of the old. He went abroad in quest of fresh specimens. He founded and housed a museum the like of which is not elsewhere.

C. Y. White, the first pathologist, was succeeded by Dr. Herbert Fox, whose studies and publications have proven Penrose's belief that a zoölogical garden may be not merely an exhibit, but a school. having as its main function, contributions to science. His membership in the Park Commission was incidental to his presidency of the Zoo and for the purpose of correlating the interests of both.

His struggle for health was amazingly successful. When after a period of intensive work his warning came, he hunted, fished and explored; in the Rockies, the uplands of the South, once in Venezuela.

After months of life in the open he came back well. In the spring of 1920 his warnings came and more urgent than ever before—he planned a longer trip than usual, but was held all that summer by the illness of his brother. Nights and days of unremitting care accomplished the impossible. None knew better than Charles Penrose that he was giving his own life for that of the Senator, and that when the time of rest came the sun and air could no longer bring back that which was so far spent.

A banker, after a dinner of pre-Volstead times, spoke slightingly of Abraham Lincoln "because he left a small estate." Lincoln left a continent in peace and honor to now one hundred and ten million people. No larger legacy is recorded in history. Even from the narrow standpoint Penrose would have commanded the banker's respect. From the broader one, to many millions he left a longer life, a better health, forests, game in abundance, a zoölogical garden of first rank contributing largely to science and a department of research.

Penrose was strikingly handsome, standing six feet and of powerful build. Till within a year of his death, he presented the color, bearing and appearance of rugged health. He was unemotional, undemonstrative; on the birth of his son, a lady whose life he had saved and who spoke of him as having the face of Endymion, hands of velvet and the tread of a marching regiment, said: "Aren't you thrilled at the coming of Little Boy Blue?" He answered, "He is not a blue baby; I am not thrilled; but, of course, the young of all vertebrates are interesting."

With him all policies were subject to cold deliberation. When approved by reason they were followed by prompt action, the details of which were carefully planned and carried out with a tireless persistence which neither hurried nor delayed. He loved power, but never its display. He shunned publicity and condemned with extraordinary vigor of diction those to whom it came either by choice or chance. Law-abiding, he bitterly opposed the encroachment of national authority over that of the state; and the interference of both with individual rights and privileges.

He shot in perfect form, deliberately and with deadly accuracy He was a good farmer and gardener; a good horseman; a good fisherman; an admirable host, skilled in cooking, exacting and securing the best; a good sailor. All things he did well; deliberately and efficiently.

In one of his many hunting trips he was attacked by a grizzly bear. Because of a garbled account of this in its magazine, he resigned from the Geographical Society and wrote the true story for *Hunting and Conservation*, the book of the Boone and Crockett Club. In this story the man is revealed. He writes—

"On September 1, 1907, my brothers Boies and Spencer and I had made a camp on the mountains lying between the Middle and South Forks of the Flathead River in Montana—about five miles south of the line of the Great Northern Railroad. The country was very rough and difficult of access, and we saw no signs of man having been there before, except the recent trail of a small party of the United States Geological Survey in charge of Mr. A. A. Stiles, who had gone there to map the country. Our camp was situated nearly on top of the range, at this place about 7000 feet above sea level. The highest neighboring peaks were under 8000 feet. The geological party was camped about a mile away.

"At four o'clock in the afternoon I rode out with Mr. Stiles to see if we could get a deer. About two miles from camp we tied up the horses and set out separately to hunt on foot. I walked along a rocky ridge covered with scattering burnt timber, and when about half a mile from where we started a small grizzly appeared, about seventy-five yards off, coming toward me. He was unaware of me; his head was down, nosing the ground. I shot at him and he ran and rolled down the side of the ridge about two hundred yards and fell dead beside a small creek. I fired two more shots at him as he ran. The country was open; nothing but masses of rocks and naked, burnt trees. No other bear was visible. I went down to the small stream beside which the bear had fallen, put my gun against a tree, and was about to take out my pocket-knife to skin him, when two grizzlies—one smaller than the other—suddenly appeared on the side of the ridge about thirty yards away. They had previously been concealed from my view by the irregularity of the rocky ground.

"The larger bear took in the situation instantly. The hair of her back became erect, she growled, crouched and came for me at a lope. As soon as I saw her I jumped for my gun and was able to fire two shots before she was on me; the last shot just as she grabbed me. She did not rear up or strike with her paws, but came at me like a dog and seized with her teeth the mass of muscles in front of the left thigh. This threw me on my back in the creek, and the gun fell from my hand. She shook the leg as a terrior does a rat; then seized and crushed my left wrist; then took hold of the right breast and pulled and shook it. She stopped suddenly and stood over me growling. For a few seconds I lay still, and then reached for the gun lying beside me. Thereupon she started again and tried to chew the top of my head through the felt hat, making several wounds to the skull. She then chewed the right side of my face and neck, one of her canine teeth going through the cheek and breaking off one of my teeth. I thought I was "all in," and was impressed by the painlessness of the proceeding, and recalled the experience of Livingstone, who wrote that he

suffered no pain at all when he was attacked and chewed by a lion. Again she stopped, and this time I made no movement. She stood there some seconds, then turned, crossed the little creek, and walked up the opposite bank about twenty yards, and fell dying against a tree stump. I saw the blood flowing from her left hip and knew that one of the shots had mortally wounded her.

"I recovered my gun and got up and aimed at the third bear, who had meanwhile been standing where I first saw him, growling and whining and with the hair of his back erect. The gun snapped, and on throwing open the chamber I found that there was no cartridge in it. I felt for an extra cartridge in my trousers pocket and found none; the two or three that had been there were gone, having dropped out in the scuffle. But the bear did not wait. He turned and with plaintive howls loped off down the ridge.

"I was unaware of the extent of my injuries and felt no pain, weakness or shock. I was soaked with water from the creek and was covered with my own blood and that of the bear. I sat down to examine the wounds; felt my pulse, which was good; and found that there was no serious bleeding. The only serious injury was that of the left wrist, which was crushed, and from which a fragment of bone projected. I washed my handkerchief in the stream and wrapped it about the wrist, and walked back to the horses. Here I met Mr. Stiles and together we returned to camp.

"I had in camp dressings, bichloride of mercury and instruments, and I carefully dressed the wounds, took a quarter of a grain of morphia hypodermatically and got into my sleeping bag. . . . An interesting point in this experience is that the bear did not rear when attacking, nor did she strike with her paws. There was no claw wound. The wounds were all made by the teeth. Perhaps the injury to her hind leg prevented her rearing. . . . I had thirty tooth-wounds. The muscles of the thigh were crushed and lacerated; the wrist-joint was opened, several of the small bones were crushed and the scaphoid bone was bitten in two, one fragment projecting from the wound; the median nerve was severed at the wrist; the hand had been perforated by teeth in several places; the breast, head, cheek and neck were bitten; and yet when I got up to take a shot at the last bear I felt no pain and was unaware of any injury. . . . I sterilized and dressed the wounds most carefully, spending three hours at it. The result was that there was no infection and no sepsis; most of the wounds healed without suppuration; and the final recovery was unaccompanied by physical impairment or disability of any account."

One hundred years from now a research fellow, passing through the hall of the medical school, may stop for a moment, arrested by the extraordinary beauty of a face painted by Julian Story with more than his usual richness of coloring and delicacy of touch: "Charles Bingham Penrose, professor of gynecology, 1892–98." Intellect of a high order, strength, determination, ability; all these the artist has written for the reading of those to come. The Fellow

may ask why has such a one left no record other than that of his brief professorship; little realizing that rich legacy, in which he himself at that moment is sharing, a legacy which grows with the passing years.

It would be well for the generations to come to have perpetuated in some permanent and actively useful form the name of one who has so largely endowed them.

Charles B. Penrose. Born, 1862. Married, 1892. Died, 1925.

A.B., 1881. A.M., Ph.D., 1884 (Harvard).

M. D. (class president), 1884, D.Sc. 1910 (University of Pennsylvania).

Resident Physician, Pennsylvania Hospital, 1885–86.

Founder and Surgeon of Gynecean Hospital, 1887–99. Surgeon to the German Hospital, 1890.

Professor of Gynecology, University of Pennsylvania, 1893–99. Retired from active practice, 1899.

Member of the Phi Beta Kappa Society; College of Physicians of Philadelphia; American College of Surgeons; American Philosophical Society; Academy of Natural Sciences; Park Commission of Philadelphia; American Association for the Advancement of Science.

President of the Zoölogical Society of Philadelphia; President of the Game Commission, Commonwealth of Pennsylvania.

Member of the Pennsylvania Society of Descendants of Colonial Governors; Harvard Club; The Union League; the Philadelphia Club; The Racquet Club; Corinthian Yacht Club; Radnor Hunt Club; University Barge Club; The Rabbit; The Jury; Principio Gunning Club, Maryland; Henry's Lake Club, Idaho; Sand Bridge Club, Virginia; Mud Hole Meadow Club, New Jersey; The Wilderness Club; The Boone and Crockett Club.

# ANNUAL ADDRESS OF THE PRESIDENT*

By THOMAS R. NEILSON, M.D.

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The College year ending on November 30, 1924, was an exceptionally busy one. Beside the regular nine stated meetings, there were two adjourned and four special meetings. The attendance of Fellows at the stated and adjourned meetings was fairly good—upwards of sixty-two, while at the special meetings the number of Fellows in the audiences left something to be desired. There has been manifest, however, a general and deep interest in the affairs of the College, and the spirit of comradeship was delightfully evident at a dinner recently given by the Weir Mitchell Entertainment Fund at which nearly three hundred Fellows were present.

The scientific contributions forming the proceedings of the College—including the Sections, which are integral parts of it—were numerous. Many papers of interest and importance will appear in the year's volume of *Transactions*.

At the stated meetings, owing to pressure of other business, only twelve papers—some of notable importance and merit—were read, three of them by distinguished invited guests.

There were three Mary Scott Newbold lectures—the twelfth, thirteenth and fourteenth. These lectures were given by Biedl, of Prague; Fitzgerald, of Toronto, and Hunter and Royle, of Sydney, Australia, respectively, and were highly instructive and meritorious—worthy additions to the fine list of discourses under that most useful and generous foundation.

The annual reports of officers and the standing committees submitted at the December meeting show the condition of the institution to be in all respects gratifying.

Your great library continues its steady growth. Contained in it, including some 21,333 unbound "Reports" and "Transactions," are 144,421 volumes. Your attention is called by the Library Committee to its embarrassment in the matter of binding. On

* Read January 9, 1925.

account of the great advance in cost it has been necessary, for lack of sufficient funds, to confine this requisite work to only important books and periodicals, and for several years to delay the binding of pamphlets and of reprints by subject. Obviously this state of affairs cannot go on indefinitely.

Under the watchfulness of the Hall Committee your building is in good order and the expense of its maintenance has been kept at the lowest possible figure.

The last volume of *Transactions*, which includes those of the Sections, is the largest ever produced by the College. Its preparation called for no little work and attention on the part of the committee and the editor.

The Directory for Nurses had another busy year, and the committeee was able to make the same appropriation from its receipts as last year ($2000.00), toward the support of the Library.

The reports of the Sections show continued activity. Much creditable scientific work was produced in all of them. It is gratifying to note a material increase in the membership of the Section on Public Health and Industrial Medicine, as well as a good attendance at its occasional meetings.

A propos of the matter of public health, it is a pleasure to remind you of the generous gift to the College, by Dr. James M. Anders, of the sum of $5000.00 to establish a fund the income of which is to be used for the purposes of the Committee on Public Health and Preventive Medicine in the performance of its duties. You may henceforth properly expect the Committee, pursuant to one of the purposes of the Fund, to bring to the College information upon material matters of hygiene and sanitation, so enabling it to raise its voice in an authoritative way and to exert its influence when expedient.

In the private sessions of the College during the year much time was taken up with the revision of the Ordinances and By-laws. Practically all of two stated meetings besides two adjourned meetings, were devoted to the work, but so far only three of the twenty-four chapters have been completed. Consideration of the next two chapters brought the work temporarily to a halt, after the College had by vote expressed its intention to make a radical change as to its meetings. With the underlying thought of stimulating the production of more scientific communications worthy of the College, it is planned that of the nine stated meetings of

the year to which we have so long been accustomed, on the first Wednesday of the month, eight shall be devoted to scientific business only, while at the ninth—the December meeting—there is to be, in addition, a short business session for the sole purpose of making nominations for officers and elective standing committees for the ensuing year.

Of Stated Business Meetings the plan provides for but two in the year—one on the Monday following the first Wednesday in January, the other on a corresponding day in May, for elections, the voting of appropriations, and for other business requiring action by the College itself.

Upon the Council is to be imposed the duty of disposing of all routine business during the year, reporting its transactions to the College.

The Committee on Revision has been instructed to prepare amendments to the remaining By-laws to bring them into accord with this plan, and is ready to report, submitting at the same time other amendments which seem desirable.

I would earnestly urge that you proceed with and complete promptly the work of revision. Your committee, thoroughly familiar with the ground, has gone over it carefully, and the results of its deliberations might be accepted and the proposed amendments adopted without extended discussion.

The supply of corrected copies of the Ordinances and By-laws is exhausted, and but few uncorrected copies now remain. There is, therefore, need for a new issue as soon as may be.

Whether the fundamental change concerning the meetings will prove altogether successful, remains to be seen. The idea of entrusting to the Council the transaction of all business not requiring action by the corporation is not a new one. It was thought of long ago, but never tried. Since it will expedite the disposal of much business, the plan will probably in this respect work out well.

The finances of the College, as shown by the reports of the Treasurer and the Committee on Finance, are in sound condition. The amount of income available for general purposes is usually barely sufficient, even with careful pruning of requests for appropriations, for annual expenses. This year the amount that will be received is uncertain, and for that reason the Committee on Finance has recommended that appropriations be now made for only half of the year.

On July 1 next, income from the College property at Thirteenth and Locust Streets will cease. The lease of the present tenant will terminate on that date. It is hoped that the property, which is now for sale, will be disposed of advantageously in the meantime.

The College badly needs more income. I have already mentioned the lack of sufficient funds by the Library Committee to do all the binding that should be done. Your building is large and the cost of its upkeep great; taxes and the care of the adjoining garden require a considerable sum; and there are other recurring demands for the expenditure of money which the present income will not permit. In the very near future you may expect to be called upon to meet pressing needs in connection with the Library. Its constant growth and the greater use of it will demand an increase in the working force and the securing of an Assistant Librarian. For publication purposes, too, you should have more money available. This work is very costly.

Now, of course, there will be some, let us hope a material, increase in income from investment of the principal to be received when the old building is sold. But even then you will need more, and I would suggest two ways of getting it. One is to again increase the Annual Contribution of the Fellows to $30, which was the amount paid for several years up to 1915. The wisdom of this step may, I grant, be questionable, but it might properly be considered. The other way is to secure an Endowment Fund, the income to be used for the general purposes of the College, and to be appropriated as might from time to time seem necessary or expedient. Perhaps one of you might influence some public-spirited person or persons of means to make such a gift.

In the routine operation of the College you are fortunate in having the continued faithful services of the Librarian and Superintendent, Mr. Fisher, and of the Clerk, Miss Zelner, to whom an expression of appreciation is due.

Concerning Membership. During the year 22 new Fellows were elected, 11 Fellows died, 3 resigned and 1 forfeited his Fellowship. One Foreign Associate Fellow died and 2 were elected. There was a net gain of 7 Fellows, and 1 Associate Fellow.

The list on December 1, 1924, included: 504 Fellows; 20 Associate Fellows (13 American and 7 Foreign); 5 Corresponding Members. Total, 529.

Of the 504 Fellows, 459 reside in Philadelphia or in its immediate

vicinity in Pennsylvania; the remaining 45 have become non-resident. The year's roll of the dead includes:

Henry Leaman, elected a Fellow in February, 1887; born in Leaman Place, Lancaster County, Pennsylvania, on July 3, 1839; graduated from Jefferson Medical College in 1864. An acting assistant surgeon in the U. S. Army, for a time in the hospitals at Gettysburg, Dr. Leaman became after graduation prosector to the professor of anatomy in the Jefferson Medical College, and later was surgeon to the Charity Hospital.

A well-known and successful practitioner, he was a younger member of an interesting group of men who will be remembered by the older Fellows, and who centered about a noted scientist and physician—Albert Frické, in his day, too, a Fellow of this College. That group, long-time intimates, included among others Drs. R. J. Dunglison, Richard J. Levick, Thomas G. Morton, and, above all, the great Leidy. Dr. Leaman retired from practice some five years ago, returned to the place of his birth, and there died on December 20, 1923, at the age of eighty-four years.

W. Wellington Woodward, elected to Fellowship in 1913, was born in West Chester, Pennsylvania, in 1880. He was a graduate of Haverford College, and studied medicine at the University of Pennsylvania, receiving his M.D. in 1905. After serving as resident at the Episcopal Hospital, he returned to his native town to practise, receiving an appointment on the staff of the Chester County Hospital, where he became assistant surgeon.

It was there, while operating upon an infected patient, that he scratched a finger, and from this wound became badly infected, dying of pneumonia on January 13, 1924. An attractive, straightforward man, Dr. Woodward was an earnest worker, with distinct ability, and devoted to his profession. In the World War he served with credit in the Medical Corps of the U. S. Army in France.

Henry Dorrance Beyea died in his fifty-sixth year on January 19, 1924, at Ware Neck, Virginia. A graduate of the University of Pennsylvania, he was elected a Fellow of the College in 1896. Dr. Beyea devoted himself to gynecology and abdominal surgery, and taught, first as instructor and later as associate in gynecology, in the University of Pennsylvania for a number of years. For a long time he was also assistant surgeon to the Gynecean Hospital.

At one time he was chairman of a Section on Gynecology that for a few years existed in the College.

He was deservedly distinguished in his special work. He devised an operation of gastropexy, afterward known by his name, for the relief of gastroptosis. This was first described in the report of a case by Dr. Alfred Stengel and Dr. Beyea, read before the College in 1899.

Albert Philip Francine, a graduate in medicine of the University of Pennsylvania, was elected a Fellow in October, 1903. At the age of fifty-one he died on March 17, 1924. He distinguished himself by his notable work in pulmonary tuberculosis, and was on the staff of the Phipps Institute, and visiting physician to the Department for Tuberculosis at the Philadelphia General Hospital. Successively Dr. Francine was chief of the State Dispensary for Tuberculosis in this city, chief of the Division of Tuberculosis of the State Board of Health, and at the time of his death was clinical director of tuberculosis in the United States Veterans' Bureau at Washington.

At the University of Pennsylvania he taught first as instructor and later as associate in medicine.

In the World War he served with distinction in the Medical Reserve Corps, first at camps in this country and then in France, along lines of sanitation and in the gas hospitals.

Dr. Francine was brilliant, and contributed much to the literature of pulmonary tuberculosis and diseases of the chest. He read a number of important papers on these subjects before the College.

Macy Brooks was elected a Fellow in October, 1907. He lost his life in an automobile accident near Alexandria, Egypt, on June 4, 1924. He was in his fifty-second year.

Early in his professional career he specialized in venereal diseases and genito-urinary surgery, later receiving an appointment as assistant genito-urinary surgeon to the Philadelphia General Hospital. Although in his specialty he showed marked ability and was a well-educated physician, we knew him but little at the College.

Duncan Lee Despard was elected a Fellow in January, 1908. A graduate of Jefferson Medical College, he served most creditably a term as resident physician at the Episcopal Hospital, where, as one of my residents, I had the opportunity of observing his fine

qualities. Returning to Jefferson, Dr. Despard became connected with the surgical departments of the college and of the hospital in minor positions, and by virtue of his faithful work and his marked ability rose to the rank of assistant professor of surgery and surgeon to the Hospital. He was also for a number of years surgeon to the Methodist Hospital as well as to the Abington Memorial Hospital.

He was a good, practical surgeon, an exceptionally good diagnostician, and had conspicuously that rare and priceless gift of good judgment.

Dr. Despard was a loyal and interested Fellow of the College. As a writer he was not profuse in his contributions, but when he did write his work was excellent and worth while.

The career of this fine, useful man was cut short in his fifty-sixth year, on August 5, 1924, when he was shot down in his office by an insane former hospital patient, dying on the evening of the same day—a horrible ending for one whose life had been characterized by gentleness, self-sacrifice and noble work.

The shocking death of Robert Grier Le Conte occurred on August 6, 1924. I shall leave it to his memorialist to tell you on another occasion the story of his life, and shall mention only briefly the activities in the College of this excellent and honored surgeon and widely-loved man.

To the scientific work of the College, Dr. Le Conte contributed from time to time some interesting and valuable papers.

In the management of the College he was for a long time interested and faithful. For four terms he was elected a councillor, and was one of the original trustees of the Nathan Lewis Hatfield Prize and Lectureship Fund.

George A. Piersol, elected a Fellow in May, 1883, died after a long illness on August 7, 1924, at the age of sixty-eight.

A memoir of this distinguished and learned teacher and writer, beloved by students and colleagues, successor to Leidy in the chair of anatomy in the University of Pennsylvania, will be prepared by one long associated with him in his work.

Morris Booth Miller died on November 5, 1924, in his fifty-seventh year. He was elected to Fellowship in October, 1910. A graduate of the University of Pennsylvania, Dr. Miller, soon after a hospital internship, applied himself to surgery. Although

connected with other hospitals, he was chiefly identified with the Philadelphia Polyclinic as a professor of surgery, teaching there for a number of years, and continuing in the same chair after the merging of the Polyclinic with the Graduate School of the University until, on account of ill-health, he resigned in 1922, and was made emeritus professor. He did a great deal of valuable work both as a surgeon and a teacher and was a devoted Fellow of this College.

In the World War Dr. Miller served with great credit for nearly two years in the Naval Medical Corps with the rank of commander, his duties being on board a transport.

An attractive, considerate and popular man, he was ever cheerful even in spite of bad health and of the threatening sudden ending which finally came.

Alexander W. MacCoy, who was elected a Fellow in November, 1886, died on November 19, 1924, in his seventy-eighth year. Dr. MacCoy was a prominent laryngologist, once president of the American Laryngological Association, lectured on his specialty at the Woman's Medical College of Pennsylvania, and for some ten years was professor of diseases of the nose and throat at the Philadelphia Polyclinic. He served also for some years as surgeon for diseases of the nose and throat in the out-patient department of the Pennsylvania Hospital, and later became consulting laryngologist to the Bryn Mawr Hospital.

An accomplished man, he left behind him a distinguished record in his chosen field.

John Bingham Roberts, elected a Fellow in October, 1878, died at the age of seventy-two, on November 28, 1924. On the list of Fellows he was, at the time of his death, the seventh in point of seniority.

It is to be the privilege of the writer of a memoir to picture the life and activities of this widely-known teacher, writer and surgeon, and interested member of many societies.

In the College Dr. Roberts was always active. Not only was he a frequent contributor of interesting papers, taking part as well in the discussion of others, but he was conspicuous in his work for the College, serving for some ten years as chairman of the Committee on Finance and for some four years as treasurer, until compelled by illness to resign.

Major-General William Burney Bannerman, an Associate Fellow since 1908, died in Edinburgh, Scotland, at the age of sixty-five, on February 5, 1924. This distinguished man served for years in the Indian Medical Service of Great Britain, and became, in consequence of his diligent work in connection with the plague in Calcutta and in research work at the Bombay Laboratory, an eminent authority on the subject. For his meritorious work he was given the C. S. I., and was made honorary physician to the King.

Fellows of the College: this is the last time that I shall have the pleasure of addressing you as your President. I can find no words to express my high appreciation of the honor you conferred on me by choosing me to serve for the full period permitted by the By-laws in the highest office of this venerable and famous institution —an honor, that as long as I live, I shall always cherish. It has been an unceasing pleasure to have served you. In meeting the great responsibilities and discharging the duties of my office, I have endeavored to give of my best. No one more than I has been conscious of my short-comings. I am most grateful for the unvarying kindness and consideration which you have at all times so generously shown me.

# SOME SUGGESTIONS TO THE FELLOWS OF THE COLLEGE BY THE NEWLY ELECTED PRESIDENT*

By HOBART AMORY HARE, M.D.

I am well aware that it is an innovation for the newly elected President of the College of Physicians to make an address at the first meeting at which he is called upon to preside. Nevertheless, it seems not out of place to present certain facts and theories concerning the College which may be of service to this ancient and honorable body.

In the first place, while it is true that times change and we change with them, it is also true that this College, adjusting itself to the world of today, must nevertheless adhere to the principles and the ideals of its founders and by wise conservatism afford an example to the profession in general as to conduct and discipline. It must, by the character of its Fellows, engender among young medical men an ambition to be one day worthy of Fellowship and so stimulate them to add to medical knowledge and culture. For this very reason it must be careful in its selection of Fellows. I would call attention to the fact that until three or four decades ago it was customary for Fellows to propose men who had attained some eminence or held promise of good things, and that anyone applying for Fellowship was considered as one acting in bad taste. It is for this reason that we have propositions for Fellowship and not applications for Fellowship. This is a point worthy of emphasis on the part of your executive, and perhaps, I may say, worthy of remembrance by the Fellows in general.

Having served many years on the Council, either by election or by appointment, I may point out that in many instances it has seemed as if proposers for Fellowship sometimes sign the official blanks because they are asked to, and often for no other reason than

* Read February 4, 1925.

this, or because of the fact that they know of nothing *against* the candidate. Often this is done because the Council is to act in the matter, and so, to use the vulgar expression of the day, they "pass the buck" to that body, and when the Council fails to recommend the person, his proposers feel annoyed because their signatures seemingly have not carried enough weight to ensure a recommendation for Fellowship. I make bold to assert that the primary responsibility rests upon the signers, that is, the Fellows, themselves, and that until those who are asked to sign regard this act not as a favor rendered to a friend but as the duty of a trustee of a great institution, not only made up of buildings and grounds and a great library, but also designed to uphold certain high ideals and standards in our profession, the institution will suffer. The question to be asked himself by each signer of a proposition is not, "Is this a good thing for the candidate?" but rather, "Will the election of this man be a benefit to the College?" The question is not, "Is there any reason why this man should not be elected?" but rather, "Is there one or are there many reasons why he should be elected?"

Large as the Council is in numbers, it is not possible for it to know of the career of each person proposed. If his accomplishments make him worthy, and the Fellows proposing him believe him qualified, they should take enough interest, not in the candidate but in the College, to communicate with several Councillors and give them facts. When this is done much humiliation for proposer and candidate will be avoided, because the man will be practically sure of recommendation unless evidence is presented, unknown to the proposer, which acts as a bar.

The question has been asked what constitutes qualification for Fellowship? This is now answered by a committee appointed of the Council, which I quote as follows:

1. That the candidate for Fellowship should not be considered qualified because of his promising future, but rather because of his accomplishments.

2. That in addition to qualifications as to character and behavior, stated in the By-laws (Chap. I, Sec. 5), the candidate should have made some contribution of recognized value to medical literature, or that he be actively engaged in medical teaching, or that he hold some hospital position of importance, or that he should have shown outstanding ability as a practitioner.

3. That a Fellow who signs a proposition for Fellowship shall feel

it his duty to inform members of the Council of his reasons for making the proposition in addition to the formal letter which must be sent before the Council takes action.

The College adopted as a guide this—

METHOD OF SELECTION. 1. That each Councillor shall be provided with a list of all candidates proposed for Fellowship.

2. That the Council need not finally dispose of a candidate when his name is first presented for formal consideration at the end of six months, but may postpone final action six times, at the end of which period, if the candidate has not been recommended for election or been rejected, his name shall be removed from the list and his proposers notified.

3. A candidate rejected, or automatically dropped, after six considerations may be reproposed at the end of two years from the date of rejection or from the date his name was removed from the list.

4. That a candidate must receive four-fifths of the votes cast at a Council meeting in order that he be recommended to the College for Fellowship.

May I present another aspect of College affairs? I have heard it said that the meetings of the College are uninteresting. Whether they are such from a medical standpoint largely depends upon the Committee on Scientific Business. If they have been so in the past I trust they may be better in the future. But the other side of the matter is this, namely: This College is a corporation with approximately a million dollars of property and a library which is one of the greatest in the world. These facts require the transaction of business of great importance and the consideration of many financial problems as well as those of expediency. Those who are really interested in the College ought to be as much interested in helping to solve questions of business and problems of administration as they are in so-called scientific communications. As a matter of fact, when the business of the College, which is its heart's blood, is to be considered, there is, in military parlance, an almost complete evacuation of the Hall, although the mind and soul of the College, which cannot exist without the blood, may have had a fairly full "occupation." The two things are inseparable, and those who wish to draw rations and do not care to help the commissary department, ought to be thankful that a relatively small number of the Fellows devote many hours and much ability to what appears to be tiresome

to the majority. Be it recalled to mind, however, that whenever a majority of the Fellows desire a change in the administration it is always in their power to put such a change into effect, although if they do so they should first ask themselves if they know enough about business, *this* business, and have the time required, to be willing to take up the burden.

Last of all, may I try to answer the question, "What is the College?" My answer is, that it is not merely a place where pretty much any type of paper can be presented; that it is not a place where honor is to be *sought* by the individual; that it is not a place where the hurly-burly of political life is to be carried on; but it is a place in which is found something equivalent to the nucleus of a cell; a place in which the nucleus of our profession is nourished by its surroundings and protected as well from envy, hatred and malice; an institution which performs many functions and tries to do them well; a place where high ideals are always at home; a place to which we turn, as does the world in general to some great cathedral, to breathe its atmosphere, to worship at its shrine, and on going out to find that doubts as to what is worthy are scattered and proper professional conduct made clear. It is a place to which the novice in our profession turns for inspiration. It is a place to which its Fellows turn as the physicist turns to the Bureau of Standards in Washington, save that there are found weights and measures and rigid rules, while here there exists a spirit whereby we weigh our acts and steer our course.

May I make a plea that when a Fellow writes a paper he shall make it worthy of the College; that when he signs a Proposition he shall regard his signature as the signature of one executing a trust, and, last of all, may I express the hope that during the coming year every Fellow will feel that he is a responsible factor in the success of the institution to which he belongs.

Under Resolution adopted by the College, December 7, 1910, it directed that at stated and special meetings suitable gowns be worn by the President, Vice-President, Honorary Librarian, Secretary and Treasurer, and that the officials be seated upon the platform. In obedience to this rule, as far as physical conditions will permit, I have asked the Vice-President to occupy the Chair on the left at every meeting, and, should he be absent, have asked the Honorary Librarian, or in his absence the Treasurer, to occupy the same position in order that all three chairs be filled.

# THE SO-CALLED RECTICULO-ENDOTHELIAL SYSTEM: ITS RELATION TO PHAGOCYTOSIS, DEFENSE PROCESSES, LIPOID AND PROTEIN METABOLISM, DESTRUCTION OF RED CELLS, AND TO NEOPLASMS*

By E. B. KRUMBHAAR, M.D., Ph.D.

(From the Laboratories of the Philadelphia General Hospital.)

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I. Introduction. For many years it has been known that there were certain cells scattered through the body that had important functions relating to phagocytosis, increased blood destruction and possibly immunity production. Sporadic and disconnected observations, often concerned only incidentally with the activity of those cells, appeared in the literature, until in 1913, Aschoff and Landau proposed "to group together a special type of cells of wide distribution in the mammalian organism as a system of reticulo-endothelial cells," which, as Kiyono has shown, "can be demonstrated throughout the entire animal series from the mammals to the cyclostomes." On this account and for the sake of convenience the system is sometimes spoken of as Aschoff's, though in fairness to that investigator it should be said that he has always given emphasis to the important work that preceded his in this field. As the functional position, unity, independence and scope of these cells, however, are open to some question, it seems safer still to speak of the so-called reticulo-endothelial system. Whether or not this terminology is justified, time alone will show; but in the meantime the statement of the proposition will materially have aided progress.

Although eleven years have passed since this concept was proclaimed, during which time many observations have added to its importance, recognition of the system does not seem to have made much progress in this country. It is for that reason that I wish

* Read January 7, 1925.

to speak of it tonight, although I shall add very little that is original or new, and only be able to mention briefly its status in anatomy, physiology and pathology.

II. Cytology and Phagocytosis. First, as to the form and distribution of these cells. In the seventies the French histologist, Ranvier, described a branching connective-tissue cell with oval nucleus and finely granular protoplasm, which he called a "clasmatocyte," on account of its tendency to break off particles which he thought furnished nourishment to the tissues. Although he attempted to identify these cells in the tissues by special dyes, he practically failed, and it was not until 1904 that they were definitely segregated by Ribbert in his interesting observation on the retention of carmine by tissues. When one injects carmine in an animal, either by intravenous, intraperitoneal or subcutaneous routes, the coloring matter is not entirely eliminated by the kidneys, but a certain part is held in the organism. This retention does not occur haphazardly in the tissue, but is peculiar to certain cells or rather to a definite cellular system. In the glands of external secretion the carmine is found only in the renal and hepatic epithelium; but it is present in greater amounts in the cells of Kupffer in the liver and in the endothelium and reticular cells of the spleen and the lymph nodes; in the endothelial cells of the bone-marrow; in the bloodvessels of the medulla; in the adrenals and thymus, and, finally, in certain branching cells of connective tissue which Ribbert identified with the clasmatocytes of Ranvier.

Ribbert, recognizing the importance of this observation, which was similar to the earlier ones of von Recklinghausen and of Ponfick on the absorbtion of cinnabar, extended his experiments to various physiological and pathological processes, and found that the retention of carmine is very markedly influenced by morbid processes, both local and general. It is at the minimum in animals weakened by cachectic diseases and, on the other hand, is augmented in certain tissues which are actively proliferating, as for example in neoplasms. Ribbert also demonstrated the capacity of these specific cells to absorb iron, lipoids and many other substances. Renaut's rhagiocrine cells, Marchand's adventitial cells, Dominici's lymphoconjunctive cells, Metchnikoff's macrophage, Maximow's polyblast and Aschoff and Kiyono's histiocyte are probably all different names for the same or closely related cells.

From another point of view, Metchnikoff made important con-

tributions to our knowledge of this system in his well-known works on inflammation and immunity. Distinguishing between the microphages (the ordinary leukocytes of the blood) and the macrophages, large cells also having the power of phagocytosis, he not only showed a surprising acquaintance with the complex distribution of these cells through the body, but also with their varied functions. He spoke of their practically amounting to a digestive system for the blood cells; in other words, an important part of the hemolytic side of what I have recently called "the hemolyto-poietic system." He also attributed to them the formation of agglutinins, coagulins and ferments, of utmost importance to the defense mechanism of the body.

Following the introduction into experimental medicine of various benzidine dyes by Ehrlich, vital staining became a popular method of research. Bouffard was the first to show that certain connective-tissue cells took up those dyes; but Goldman, using pyrrhol blue, in very careful and extensive studies, identified them with Ranvier's clasmatocytes and confirmed and extended the work of the earlier investigators. He saw that in the course of digestion the vitally stained cells abounded in the intestinal coats; in the fasting animal, on the contrary, the intestinal wall was almost colorless. A female intensely colored by vital staining became decolorized when she became pregnant; the color was not eliminated, but accumulated in the uterus, especially in the placenta. An accumulation similar to the vital stain was observed in the mammary gland during lactation and it was found also in the granulation tissue and in cancer stroma.

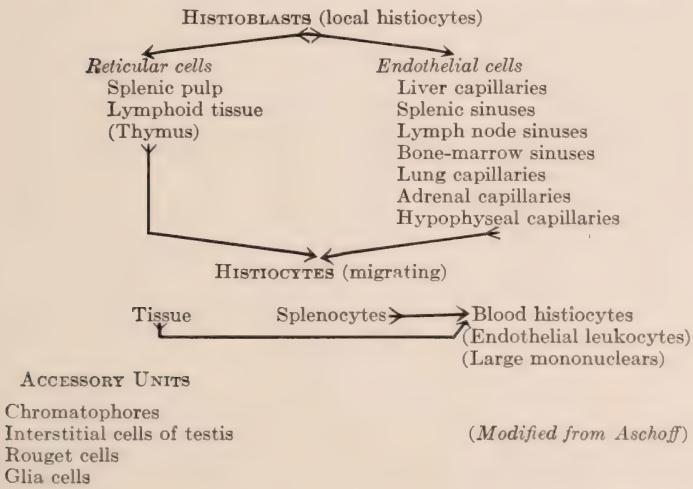
Aschoff and his collaborators, Kiyono and Nakanoin, reviewed the status of the many cells concerned in these activities in a wide range of experiments. While it is still doubtful what should be properly included in the reticulo-endothelial system, Aschoff has tabulated in ascending order six mesenchymal elements according to their behavior with vital dyes:

1. *Ordinary endothelium* of blood and lymph vessels, which only take dye in extreme cases and in the finest granules.
2. *Fibrocytes,* which take dye somewhat more easily.
3. *Reticular cells* of spleen and lymphoid tissue which take dye readily and deeply, but less than the three remaining groups.
4. *Reticulo-endothelial cells* of spleen and lymphoid sinuses, bone-marrow, adrenals and hypophysis capillaries and Kupffer cells.

5. *Histiocytes* or clasmatocytes.

6. *Splenocytes and blood monocytes.* The first two groups Aschoff rejects from the system on account of their resistance to the dye and their fixed qualities. The remainder it would seem possible to group in a table, allowance being made for the possibility of a free transition from one type of cell to another, the extent of which change is by no means settled. From all this work we may retain the fundamental idea that there seems to exist widespread through higher animals a well-characterized cellular system, easily demonstrated by vital staining and comprised essentially of reticular and endothelial cells. This group of similar though not identical cells forms a vast complex, which sends outriders through all parts of the organism, including the circulating blood. The morphological characters of these cells has been known for a long time; the new contribution is the conception of biological unity of these cells, which if true will give us the right to speak of a reticulo-endothelial system.

TABLE.—SO-CALLED "RETICULO-ENDOTHELIAL SYSTEM"




(*Modified from Aschoff*)

The facts which show the physiological and pathological importance of this system are accumulating. They will be considered here under four separate heads.

III. Role of the So-called Reticulo-endothelial System in Defense Process. The retention of coloring matter and other

particles has already been noted as an important property of the reticulo-endothelial cells. The degree of the retention varies con-considerably, both according to the chemical constitution of the coloring matter, and especially being influenced by the phase of the solution. In dispersed solutions there is generally a marked retention in all the units of the system; according as the concentration becomes greater, the extent of the vital staining diminishes. It is at first the histiocytes and the reticular cells of the lymph nodes which stop taking up stain; next the Kupffer cells, and finally, in the much less-dispersed systems, the spleen only remains sensitive. Herein lies a very important observation: This differing sensitivity of the reticulo-endothelial cells from the point of view of absorption is without doubt the expression of a certain autonomy of the different territories of the system.

Excluding the physical and chemical characters of the solution, the degree of retention depends in considerable proportions on the momentary functional state of receptivity of the cell. Vital staining of the intestine well illustrates this fact; its intensity at the moment of digestion is due not so much to the accumulation of reticular cells, as Goldmann believes, but to an exalted receptivity. The actual number of the phagocyting cells is hardly greater at this moment than when the animal is fasting (Kuczynski).

From another point of view the interesting observation has been made that the reticulo-endothelial cells can take up a stain or a colloidal metal to such a point that they become refractory to every other substance. It is on this fact that the "blockage" experiments are based. For instance, if Kupffer cells are loaded with parenterally injected collargol, they will then be less able to handle the products of a hemolytic poison, with a consequent reduction in the ensuing jaundice (Lepehnel). But it should be said at once that this method is not altogether reliable. First of all, it is very difficult to obtain a complete blockage of all the reticulo-endothelial cells in a given territory, because these cells are often in very different stages of receptivity to one element or the other, and even if the blockage succeeds in an ideal manner, it cannot be of long duration; we have already seen that the reticulo-endothelial cells are constantly being renewed and this renovation is of course more active and rapid when the cells are blocked. In fact, Kiyono showed that blockage is the best means of provoking an abundant irruption of reticulo-endothelial cells into the blood.

The absorption of stains and colloid metals and other electro-negative particles (Paschkis) is only one particular manifestation of a much more general functional property, namely, phagocytosis. It has been known for a long time that many bacteria and parasites injected intravenously are retained in large numbers by reticulo-endothelial cells (Wyssokowitsch). Under these conditions it is not surprising that the system should play an important part in many acute infections. In tuberculosis (Foot), typhoid fever (Mallory), leprosy, kala-azar, oriental sore, rhinoscleroma, actinomycosis and sporotrichosis these cells play a leading part in the tissue reactions, either locally or, as in several of them, where the lesions in the spleen, bone-marrow, lymph nodes and liver demonstrate their intimate connection with the reticulo-endothelial system. These facts have not escaped the histologists who have studied these diseases. The rôle of the system has been well expressed in the terms of Letulle: "It follows that kala-azar and oriental sore consist of a fairly specialized inflammatory lesion which is characterized by the activity of the macrophages contained in the region where the parasite is localized."

But the reticulo-endothelial system is not only concerned with phagocytosis and destruction of pathological agents, it collaborates very probably in the production of many ferments, antibodies and other substances indispensable for the defense of the organism, as was recognized very thoroughly by Metchnikoff. Recent studies have furnished very interesting facts on this point: Murata and Bieling and Isaac have brought out the rôle of the system in the production of hemolysis, after blockage in the rabbit with China ink or colloidal silver; Murata injected sheep cells and observed a considerable diminution in hemolysis; splenectomy is said to have the same action; Bieling and Isaac showed that this diminution was not due to destruction of hemolysins, but rather to lack of formation, and was most effective if "blockage" was combined with splenectomy; Stephan showed that irradiation of the spleen noticeably increased the coagulability of the blood; this experimental observation finds its therapeutic confirmation in the efficacy of treating certain purpuric conditions by irradiation of the spleen; Gay has recently confirmed previous observations that, if "blockage" is performed with sufficient thoroughness, there is a marked drop in the power of the animal to form antibodies.

This action of the reticulo-endothelial cells, both phagocytic and

fermentative, suggests the idea that they not only intervene in the local reaction of the organism against bacterial invasion, but also take part in the production of general immunity. This view is supported by recent studies of Besredka and Delater, which tend to show that immunity is due not to a humoral production of antibodies, but to a local refractory state of certain cellular systems. This argument cannot be followed further here, however.

IV. Metabolism of Lipoids and Proteins. The rôle of the reticulo-endothelial system in the metabolism of fats and especially lipoids has been demonstrated in certain experimental conditions. Anitschkow and others have found that experimental cholesterinemia of the rabbit produces an accumulation of anisotropic lipoids (derivatives of cholesterinemia), especially in the spleen and bone-marrow, sometimes in the lymph nodes and Kupffer cells. The lipoids are found in the cells which take up vital staining, that is, in the reticulo-endothelial system.

Clinical conditions which demonstrate the close connection between certain lipemias and changes in the reticulo-endothelial cells are found in diabetic lipemia, xanthelasma and xanthomata. In the first of these conditions the spleen is greatly swollen, the Malpighian follicles disappear completely and the pulp is occupied almost entirely by very large epithelioid vacuolated reticular cells. Their appearance and the histochemical reaction of their cytoplasmic content show that they are filled with substances of a lipoid nature. The number of these cells is said to be in close relation to the concentration of the lipoids in the blood. The hyperplastic reaction and lipoid infiltration do not concern the reticulo-endothelial system as a whole; changes are localized at first in the spleen, then in the liver, lymph nodes and in the bone-marrow. This localization is not, however, exclusive, as we recognize quite similar changes in elements of connective tissue in xanthelasma and xanthoma. Xanthelasma presents in the connective-tissue interstices of the skin vacuolated cells loaded with neutral fats and cholesterin esters. Xanthomata are due to a proliferation of fusiform cells, often degenerated and loaded with lipoid substances. It is evident that the tumor-like malformations correspond to a proliferation and fatty metamorphosis of histiocytic cells, such as one observes in other conditions in the spleen, liver and bone-marrow. These facts are all the more interesting because there is also an evident clinical relation between the condition and the

metabolism of the fats and lipoids. One has only to recall that the xanthomata are usually found in subjects of hepatic disease, with or without icterus, and in diabetes and pregnancy. Furthermore, the studies of Chauffard and his school, De Pautrier and Levy have shown that these tumors are accompanied by cholesterinemia.

In Gaucher's disease a related condition exists, though, as Mandlebaum has pointed out, the cellular infiltration is of a complex protein phosphorus-containing nature rather than of a lipoid nature. At first considered a "primitive epithelioma" of the spleen, Gaucher's disease appears today as a disease of the reticulo-endothelial system characterized by a hyperplastic reaction and a vacuole transformation of the reticulo-endothelial cells, involving liver, lymph nodes, etc., as well as spleen. As Mandlebaum and Downey have pointed out, the cells of Gaucher's disease can be distinguished histologically from various lipoid conditions, and although the matter is still subjudice it is probably best to exclude from this category cases in which "anisotropic bodies," myelin substances or neutral fats are found by microchemical methods in the involved cells.

V. Relation to the Destruction Blood Cells. Many years ago Ponfick showed that the "spodogenous" spleen found in conditions associated with excessive blood-cell destruction was due to the inclusion by spleen cells of fragments of red cells or products of their destruction. Since then many experiments have demonstrated, under widely varying conditions, the rôle that the cells which we now call the reticulo-endothelial system play in this process, whether they are found in the spleen, liver, bone-marrow or lymph nodes; and also the ability that the various units possess to compensate for the loss of one unit, such as the spleen (Warthin, Hunter and Pearce, Krumbhaar and Frazier). In certain species it is said to be even possible to follow this process under physiological conditions (Rous), so that it is believed that the normal procedure in the disappearance of effete red cells is for them to break up within the circulation into small fragments that are picked up by reticulo-endothelial cells, chiefly in the spleen. Certainly, when blood destruction is increased or hemoglobin solution injected, there is no difficulty in finding the resultant products (whether as hemosiderin granules or actual red cells) packed into the various sites in which reticulo-endothelial representatives are found (Pearce and Austin, Krumbhaar and Chanutin, Rous and McMaster).

Concerning the share of this system in the further elaboration of

the products of red-cell destruction there is less unanimity of opinion. That it is concerned with the metabolism of iron is indicated by the belief of Asher and his colleagues, that there is an increased loss of iron by excretion following removal of the spleen—an important element in the system. Though this has the support of work by Aschoff and Brugsch and Inger, and also of some "blockage" experiments (increased iron excretion following blockage of the reticulo-endothelial system by collargol), we were not able to confirm it in our laboratories.

The part played by the reticulo-endothelial system in the formation of bile pigment from the hemoglobin fraction of the red cell is still far from clear. Experiments by Joannovics, ourselves and others clearly showed that less bile pigment was formed under conditions of excessive blood destruction, if the spleen, *i. e.*, part of the reticulo-endothelial system, had been removed than if it was still intact. Conversely, it has been shown in a positive manner that reticulo-endothelial cells are capable of forming bilirubin outside of (as well as, by inference, inside of) the liver. Following the venerable observation of Virchow, that hematoidin—the isomer of bilirubin—was formed in old hematomas, it has only recently been conclusively demonstrated that bilirubin can be formed in heart-lung preparations (Whipple), or when the liver is totally removed from the body (Minkowski and Naunyn, Kyes and McNee, for birds, and more recently Mann for mammals) or in pure tissue-cultures of reticulo-endothelial cells to which hemoglobin solution has been added (Rich). Blockage experiments, to be sure, may sometimes fail to prevent the formation of bile pigment (Rosenthal and Fischer, Greppi), probably for the reasons previously mentioned, and it is curious from this point of view that whereas bile pigment can be found in the Kupffer cells in clinical cases of obstructive jaundice, it is apparently absent in nonobstructive hemolytic forms (Kammer). McNee has advanced the ingenious hypothesis that both the reticulo-endothelial cells (Kupffer, etc.) and the liver cells proper are concerned in biligenesis. In the bilirubinemia of obstructive jaundice both these elements are supposed to have exerted their action on the bile pigment, whereas in the bilirubinemia of hemolytic jaundice only the reticulo-endothelial cells have played their part, and in this way the difference between the direct and indirect reactions of the van den Bergh test may be explained. In addition to this, if the liver cells are considered as excretors of bile

pigment, the jaundice that follows the damage to them which is now known to occur in catarrhal jaundice is easily comprehended.

In clinical medicine the studies made on hemolytic icterus have been especially important in illuminating the rôle played by certain parts of the reticulo-endothelial system in the disintegration of red cells. Hemolytic icterus, as is well known, is a disease characterized by a retention of bile pigments (disassociated icterus in the sense of Brulé), splenomegaly, fragility of erythrocytes and anemia. The functional efficiency of the hepatic cell does not seem to be affected; there is, on the contrary, an abundant elimination of bile pigment—the bile is very concentrated and the feces are well colored throughout the disease. All these symptoms disappear with splenectomy. Although the reason for the fragility of the erythrocytes is not known, these facts permit of only one conclusion: that hemolytic icterus is due to an overproduction of bile and that this is intimately related to changes in the spleen. Histological examination of the spleen entirely confirms this hypothesis. This organ is engorged with blood, which is especially accumulated in the pulp, and there is a very intense phagocytosis of red cells and broken-down pigment. It is also known that in hemolytic icterus red blood cells are destroyed from four to six times as rapidly as in normal conditions. The pathogenesis, then, of this curious disease is evident: Hemolytic icterus is due to a pernicious activity of the splenic tissue, which is manifested in an intense destruction of fragile red cells (the hypersplenism of Eppinger). This destruction in turn induces a compensatory hyperplasia of the bone-marrow. As long as the bone-marrow can compensate for the blood-cell destruction there is no anemia; but, after a time, hemopoiesis may become insufficient and in this way the two cardinal symptoms are explained—icterus and anemia.

Certain forms of pernicious anemia present many analogies with hemolytic icterus. Here also one finds a subicterus due to an excess of bilirubin in the plasma, together with an increased elimination of bile by the liver cell. The spleen may be very similar to that of hemolytic icterus, with an abundance of blood in the pulp and marked phagocytosis of blood cells. These facts suggest that pernicious anemia is not, first of all, due to a defective function of the marrow, but to some unknown factor which causes an intense destruction of red cells followed by a fatigue of the hemopoietic organs. To combat this blood-cell destruction, splenectomy has

of course been tried; but, contrary to the results in hemolytic icterus, the therapeutic benefit in pernicious anemia is only temporary. Pathological anatomy suggests one explanation of this failure: In hemolytic icterus products of blood-cell destruction are found to be limited chiefly to the spleen (also in Kupffer cells); in pernicious anemia this phenomenon is much more generalized and is found in the Kupffer cells, lymph nodes and bone-marrow.

These two diseases, hemolytic icterus and pernicious anemia, and the experimental work previously mentioned illustrate then very well the intimate relations of the reticulo-endothelial system to the destruction of blood cells, but there is still much to be learned about this complicated subject. Much contradictory evidence has necessarily been omitted on account of space limitations and it is certainly unwarranted at this premature stage to claim that the reticulo-endothelial cells are the only agents concerned in the process of blood-cell destruction and bile-pigment formation. For our present purpose it is of little importance to know whether bile pigment is formed in the reticulo-endothelial cells themselves or in the circulating blood under the influence of ferments secreted by these cells. The essential fact is the considerable participation of the reticulo-endothelial system in the destruction of blood cells and in the metabolism of the products of their disintegration.

VI. Neoplasms. A final word about the relation of the reticulo-endothelial system to tumors should be included. Not only has the original conception of the neoplastic nature of Gaucher's never been really disproved, but there are also certain cases of "monocytic leukemia" in which the cells apparently are derived from reticulo-endothelial cells, and, like other acute leukemias, bear some of the stigmata of neoplasms. Furthermore, Aschoff has called attention to "circumscribed leukemic-like proliferations in isolated provinces of the reticulo-endothelial systems." There is no reason why these cells, like any others in the body, should not be capable of neoplastic growth, and primary endotheliomata and the reticular sarcomata of Ewing suggest themselves as obvious examples.

VII. Summary. Thus I have attempted to present to you the appearance, distribution and function of the cells constituting the so-called reticulo-endothelial system.

Their relation to phagocytosis, defense processes, lipoid and possibly protein metabolism, red cell destruction and bile formation

and neoplasms has been discussed. Although there is much contradictory evidence and much still to be learned about these cells, it is hoped that this incomplete survey will stimulate interest in this country in a subject which is pregnant with frutiful possibilities.

Much of the material for this article has been borrowed from the excellent article by Oberling in the new French journal, the *Annales d'anatomie pathologique*. I am glad to have this opportunity to acknowledge what in many passages (especially in Sections III and IV) amounts to a verbatim translation of his work. Aschoff's *The Reticulo-endothelial System* has also been freely utilized.

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## DISCUSSION

Dr. Alfred Stengel: It is difficult to discuss this paper for, as a matter of fact, there are very few of us who know anything about this subject or who can add anything to it that is worth while, but such study as I have made of publications on this topic have suggested two observations that seem to me very interesting. The first is one that applies to this topic and applies to many matters in the progress of medicine: how the discovery of a method at once opens up a tremendously wide field for

new observations, new classification of scattered facts and observations that have, perhaps, been made by individuals over long periods of years. Now, as I see the matter, the ability of these histiocytes to engulf carmine in solution and to deposit it in a granular form is the basis on which these cells have been recognized and are to be recognized now in different parts of the body in very diverse form. Dr. Krumbhaar did not allude to the fact that I have just mentioned, but I believe it is a fact that these cells have that capacity of digesting or somehow altering the carmine solution and presenting the carmine in this granular form. They do something of the same thing with hemoglobin—altering it, throwing it down in granular form, as bilirubin, and also distributing it afterward throughout the blood stream. The second thing that occurred to me in connection with this subject is the different points of view which Aschoff and his associates have given to various cellular processes that many of us have known about in one relation or another or that have been known and published for many years. For example, Mallory wrote very interesting papers on the macrophage in the pathology of typhoid fever. These observations were remarkably interesting, and yet the reaction which Mallory had to his own discovery, and all pathologists have had, was that here are some very interesting kinds of cells whose presence is excited by typhoid infection, but teleological interpretation of the thing has never been thought of. Aschoff looks upon these cells, not as interesting pathological exhibits indicating reaction of tissues to some irritation, but rather to the hyperplasia of certain types of cells which have a very definite function, which he goes so far as to indicate as digestive, metabolic, as well as immunizing, taking the latter almost *in toto* from Metchnikoff. I think Dr. Krumbhaar has done wisely in using the words "so-called reticulo-endothelial system." No one can look over the ground, and Aschoff's work in fact, without feeling certain that he has taken hold of a very interesting condition of things that pertains to different organs and parts of the body and represents a similar cellular process; but that it is all to be accepted, for example, that the endothelial cells of the bloodvessels and lymphatic channels are to be excluded in this system and that the other endothelial cells are included, or that the histiocytes are capable of producing lymphocytes, it is not necessary to discuss; indeed it is an impossibility to answer these questions. Some of the work done in this country, showing direct derivation of the blood cells (so-called mononuclears or endothelial leukocytes, as Mallory calls them) from these plasmatocytes, is very interesting. I do not know that Aschoff has incorporated that work in his discussion. There is no question of doubt at all that what Aschoff is putting forward is something of very great importance, that you will hear a great deal of it in the next few years and, therefore, I think it is most fortunate for us that Dr. Krumbhaar has seen fit to bring the whole subject before us and present it in such a clear way. I have nothing more to add to this excepting to say this, that a number of the cells that we have learned about in our pathological study in the past, Aschoff now identifies with these histiocytes or blastocytes—for example, these large endothelial cells which we know to be present in tuberculosis and the cells present in certain of the inflamma-

tory conditions of the central nervous system and various other situations, which in the older pathology we called epithelioid cells. They seem to be identified with these histiocytes and partake of their function, that of an immunizing and metabolizing sort.

Dr. Bowman C. Crowell: It seems to me exceedingly fortunate for the College to have presented by Dr. Krumbhaar in a very simple form what is in reality a very complicated subject, and to cover it as well as he has in fifteen minutes is something of value to the College. It seems to me, in my observation in the last few weeks, that the medical world in Philadelphia can be largely divided into two classes: When I have spoken to members here of the reticulo-endothelial system, one group has said to me, "What is it?" and one group said, "I wonder if there is one?" I think that conveys the attitude of the entire group. Personally, I think I belong to both groups.

I am not quite sure that there is a reticulo-endothelial system in the sense that it is a sharp-cut system of cells, and, if it is a sharp-cut system of cells, I am not quite sure just exactly what cells belong in that group. But whether or not it be a system, the concept of its being a system, the idea that Aschoff has given us, has certainly been productive of great good in stimulating further study of the type of cells to which he has directed attention. It shows the influence that words have on ideas. The cells involved in this system, whatever they be, have been studied for a long period of time here in Philadelphia, as Dr. Krumbhaar has suggested, in the Department of Research Medicine of the University, and various other parts of the world, but it has never before been conceived as a whole system. The real influence of the words on thought and work is brought out, it seems to me, also in the phrase of a "round-cell infiltration." If there is one phrase which should not be used and has had a deterrant influence on the progress of pathology, it is "round-cell infiltration," and it is this very group of cells in round-cell infiltration with which we are concerned in the study of the reticulo-endothelial system. Pathologists have looked at them with the microscope and said, "There is round-cell infiltration" in a way as though they had classified them, as if that really meant something, whereas it means nothing at all. That the cells are round may be true at the time one is looking at them, but there are many types of cells for many different purposes, for many different functions, classified together in that phrase "round-cell infiltration," and this newer classification will lead to further study and possible elucidation of their function.

Yet the study of the reticulo-endothelial system is going to be difficult in some ways, because the distribution of the cells that are involved in this system differs in different animals, so that it is not always possible to transmit to humans the conclusions drawn as the result of animal experiments. Already the concept of the system has served to emphasize old facts which were known before this idea was brought forth and has brought into prominence certain new facts. One of the principal facts that, it seems to me, is shown is in connection with the endothelial cells. To say that a cell is an endothelial cell does not sufficiently classify it. For

instance, we know that endothelial cells line the lymph- and bloodvessels, but some of them undergo further differentiation to perform more function than line the larger bloodvessels and lymphatic vessels; for example, the Kupffer cells in the liver and the list Dr. Krumbhaar showed in the slide. That has been especially emphasized in the work that has followed Aschoff's presentation.

Dr. William H. F. Addison: Viewing this important subject from the anatomical standpoint, I am glad that the speaker has included in his title the expression, "so-called" reticulo-endothelial system. As a morphological designation for groups of cells widely scattered through various tissues and organs of the body, the term reticulo-endothelial system seems to me incomplete, for, as we have already heard, besides the fixed cells to which the term specifically applies, it includes wandering cells, some of which are of undetermined origin. A complete morphological term should be used in reference to the histiocytes, which are considered to be derivatives of the reticular and endothelial cells, as well as other wandering cells of mesenchymal origin. You should prolong the term into reticulo-endothelial-histiocytic-mesenchymal system, or something of that nature. Here is an attempt to incorporate in one so-called system all cells having in common the function of phagocytosis. If one is using a functional criterion, it might be better to use a term denoting function, such as "phagocytic system." Under this title the various morphological entities could be aggregated as our knowledge of its components enlarges.

My interest in this subject dates from 1912, when I first saw in Ehrlich's laboratories blue mice and red mice which had acquired these colors after injection with colloidal dyes, such as trypan blue and trypan red. Great advances in our knowledge of phagocytic cells have been made with these and similar dyes. We use them now in our student classes to demonstrate the phagocytic potentiality of the Kupffer cells of the liver, of both fixed and wandering cells in the spleen and lymph nodes, and of free cells everywhere within the areolar connective tissues of the body. I noticed in one of the charts that the interstitial cells of the testis were included as doubtful members of the system. Several years ago Dr. Thorington and I showed that they were not phagocytic, but that between them, here and there, were wandering connective-tissue cells which were capable of picking up the blue colloidal particles of the injected trypan blue.

Undoubtedly all these phagocytic elements are important in the defences of the body. It is already known that there is such a thing as differential phagocytosis, certain groups of cells being capable of ingesting substances while others are not. So they have a different physiology and no doubt they have a different pathology. Further study of this subject, which has been so clearly presented tonight, is sure to yield valuable clinical results.

Dr. Krumbhaar (closing): Although Dr. Addison was looking at me when he spoke of the questionable advantage in the use of such terms as "reticulo-endothelial system," I am sure that he does not hold me responsible for their invention or concerned in their maintenance. I quite agree

with him as to the importance of terminology in defining the subject under discussion, but I think in this case it could be more profitably discussed in the quiet conference of a few than in such an assemblage as this. I will say, however, that whether or not this particular term is destined to survive, it unquestionably has already aided progress by offering a nidus about which work and thought can crystallize. The part of the system with which I was mainly concerned, namely, its relation to blood-cell destruction and bile-pigment formation, affords other examples of the principle that Dr. Stengel called attention to, namely, the importance of a new method. For many years opinion has been divided as to whether bile pigment was formed only in the liver and whether the liver excreted urobilin as well as bilirubin. These important questions have been settled recently by the development of new methods. Extrahepatic biligenesis has been conclusively demonstrated by the very ingenious method of Mann, by which he can extirpate the liver in mammals, and at the same time by Rich, of Johns Hopkins, by adding hemoglobin solution to pure tissue cultures of reticulo-endothelial cells. These two together I think confirm the conclusions of Whipple that the extrahepatic formation of bilirubin is a positive fact. The third example is the work of Rous and McMaster, of the Rockefeller Institute. By hitching a bag to the common bile duct, they could obtain uncontaminated bile over long periods of time. They thus showed that urobilin was not obtained unless the bile was contaminated, due to incomplete and unsatisfactory methods. One final word as to what Dr. Stengel said about the use of the term "reticulo-endothelial system." Aschoff himself has called attention to one of the weaknesses in calling this group of cells a system, when he arbitrarily distinguished between certain types of endothelium and the ordinary endothelial lining of blood and lymph vessels, which even in his own experiments only took up a small amount of dye. It would seem to me more logical to call all endothelial cells contributors to this process, looking upon the less active participants as accessory members.

# THE CLINICAL IMPORTANCE OF THE MYOCARDIAL RESERVE*

By WILLIAM D. STROUD, M.D.

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It is impossible to overemphasize the importance of a correct estimation of the myocardial reserve, from the standpoint of a physician in any branch of modern medicine. Naturally, its estimation is the greatest problem for those specializing in diseases of the cardiovascular system; but we must remember that upon it often depends the life of a mother and infant, or the decision of active or nonactive surgical procedures. The neurologist and cardiologist are constantly puzzled as to what extent the myocardial reserve is playing in cases with symptoms bordering on each of their separate fields of diagnosis and treatment; while, needless to say, its estimation must be a factor in the majority of patients seen by the general practitioner.

To those specializing in cardiovascular diseases this paper will, no doubt, prove disappointing, as it contains nothing new or startling for those whose work makes it necessary or has permitted them to keep abreast of the changes, and reasons for such changes, in the attitude of our profession toward the diagnosis of heart disease during the past fifteen years. It is with the hope that a review of these changes may prove of interest to those not having such an opportunity that this paper is presented.

In reviewing the literature of fifteen or twenty years ago one cannot help but be impressed with the importance placed upon murmurs and the intensity or character of the cardiac sounds in prognosticating the future of a diseased heart. Today the average student—be he a graduate or undergraduate—upon visiting a heart clinic will be found eagerly rushing from one case to another, listening to and discussing the character and importance of murmurs. To them that is the *sine qua non* of the diagnosis, prognosis and

* Read February 4, 1925.

treatment of heart disease. Certainly, murmurs are of importance, and their depreciation is being overdone by many clinicians; but let *us* attempt to take the middle ground, and give them their relative importance as aids in estimating that which, most of all, we wish to know—the myocardial reserve. Let us remember that a systolic murmur at the apex or base, with only questionable cardiac enlargement, may be of great importance in elderly people or during active infections, and practically of no importance in youth in the absence of infection. Let us remember that in our profession it is almost impossible to generalize, and for the physician the words "always" and "never" should not exist.[1] The history, physical signs and laboratory reports must be interpreted separately for each individual case, and statistics are only of value in giving us suggestive leads toward a more accurate interpretation of the condition of each individual patient.

Before the World War any patient complaining of breathlessness, palpitation, fatigue and precordial pain must needs have disease of the heart, in the mind of the average physician, no matter what the physical examination revealed. The "effort syndrome"—whatever its etiology may finally prove to be—has revealed the fallacy of this attitude. Quoting Paul D. White: "Breathlessness, tachycardia, cyanosis and heart pain do not alone justify the diagnosis of heart disease, as they are found in a variety of conditions—convalescence, fear, fatigue, etc.—when the heart is perfectly sound." An accurate, painstaking history is of great importance in the estimation of the myocardial reserve, but most important of all is the proper interpretation of such a history. After months of suffering from angina pectoris, Sir James Mackenzie died as recently as January 26, of this year. Let us resolve that as a tribute to his memory we shall, to the very best of our abilities, take careful histories in an effort to discover the early symptoms of disease, and place with meticulous care the proper interpretation upon each symptom found.

Frequently we hear the terms "poor muscular tone" and "weak heart sounds." If one will think of the number of mediums through which heart sounds must pass, one cannot help but be struck with the chance of error in determining the character of the myocardium by the intensity of the heart sounds. The pericardium, the pleura, the lungs, the chest wall, the skin, the stethoscopic bell, the stethoscopic tubing, the physician's auditory apparatus(?) and finally his interpretation of sound, may, one or all, effect the final interpreta-

tion. If we listen to the heart sounds of a thick-chested athelete and to a thin-chested child with endo- and myocarditis, in which will we find the heart sounds the loudest? We certainly must not attempt to interpret the myocardial reserve upon the intensity of the heart sounds, except in sudden changes in the case of those whom we have been able to examine from day to day, and thus are able to approximately estimate the normal intensity of that individual's heart sounds.

Again, in the cases of low blood-pressure, with or without so-called "weak heart sounds," we have been at fault in our estimation of the condition of the myocardium. Hundreds of men have been sent to the United States Veterans' Bureau with the diagnosis of "chronic myocarditis" based upon a history of breathlessness and these two physical findings alone! We must admit that we are realizing, more and more, that the systolic blood-pressure alone gives us very little idea as to the myocardial reserve. Let me qualify this statement by excepting the knowledge obtained of probable changes in the myocardium in patients with constantly elevated blood-pressure, or by a sudden fall in the systolic pressure during the course of pneumonia and other acute infections, or long-standing hypertensive cases. In these instances, however, accompanying signs of circulatory failure simplify the proper interpretation of the lowered systolic pressure.

To the average physician an irregular rhythm of the heart means serious disease of the myocardium, and yet the two most frequent arrhythmias, namely, sinus arrhythmia and multiple premature contractions, or so-called extrasystoles—in youth at lest—are of almost no diagnostic or prognostic import from the standpoint of the myocardial reserve.

So far this paper has been destructive. If you have followed me, your faith in those findings which you were taught in medical school, and which have been emphasized by the best recognized of the older writers as indicative of poor myocardial reserve, have been questioned. How, then, are we to estimate whether or no the heart will stand additional burdens placed upon it, or the cause of various symptoms of which our patients complain?

As we have already emphasized, let us place a proper interpretation upon our history as a result of our physical examination and the findings with certain instruments of precision, namely, the roentgen rays and the electrocardiogram. Let us inquire dili-

gently for evidence of infection in the past or present which may have damaged the circulatory system, such as acute rheumatic fever, chorea, scarlet fever, typhoid fever, syphilis and chronic foci of infections. A familial tendency toward disease of the circulation with the various indiscretions of life, which we believe tend toward early vascular changes, are of importance. This may seem obvious, but is too often omitted in the rush to listen for murmurs. Mackenzie[2] says: "It is one of the curious matters in medicine that the commonplace and self-evident are the things which are the most frequently ignored. I am repeatedly told by experienced physicians that the views here expressed are common knowledge and that everyone knows all about them. But if justification were needed for insisting upon this line of observation, we have but to observe how the profession employs this common knowledge." Barringer[3] claims that "the best way to judge of an organ's capacity is to set it doing its own particular work and base our judgment upon the result of such experiments." This sounds simple, but we find it to be just as difficult as the attempts to estimate the ability of kidneys to do their work. The circulation is a complicated mechanism, and the myocardial reserve of the heart is only one factor. Hence the failure, so far, in the development of a satisfactory "exercise test." A recent careful résumé has emphasized the fact that no *one* satisfactory "exercise test" has yet been devised and generally accepted by the profession. This should not detract from the definite clinical value of observing a patient's reaction to effort, so long as proper value is placed upon it as one of various evidences as to the state of the myocardial reserve.

A routine determination of the vital capacity offers much promise in this connection. The greatest of all physical strain placed upon the myocardial reserve, excepting a lack of the proper blood supply to the myocardium, being pregnancy, brings this subject to mind under the heading of reaction to effort. Time does not permit a detailed discussion, but we must agree with the main conclusions of the Obstetrical Society of Vienna, in 1921, that in the determination as to whether pregnancy should be interrupted or allowed to go to termination, we must not so much consider the actual condition of the heart, but whether it is performing its function properly. They emphasized how rarely death occurs from cardiac failure in pregnant and parturient women. In 60,000 patients there were only 11 deaths directly attributable to failure of the myocardial reserve.

Briefly, in estimating the myocardial reserve, auscultation helps us in the following manner: Diastolic murmurs, if persistent, are practically always due to organic lesions and are therefore most suggestive of changes in the myocardium. The same may be said for truly presystolic murmurs. The presence of a true gallop rhythm at rest or after moderate effort is significant of poor myocardial reserve. The French school of cardiology places especial importance upon this ausculatory finding and confirmatory evidence is rapidly accumulating in this country.

Probably because it is the most difficult in borderline cases to determine, the dictum of the modern cardiologist, least understood and accepted, is that upon the determination of the extent of the enlargement of the heart depends the truest estimate as to what extent the myocardial reserve has been encroached upon. In other words, any enlargement of the heart which is demonstrable means damage to a greater or less degree to the myocardium and a loss of myocardial reserve. Unfortunately the opposite is not true, because of the imperfections in our present methods of determination of cardiac enlargement. We are not justified in saying there has been no loss of myocardial reserve if we are unable to demonstrate enlargement, although it is much less likely under such circumstances. Eyster[4] has much to back his statement that "determination of the size and contour of the organ represents the most important single procedure in cardiac diagnosis. If we are in a position to detect with perfect accuracy the departure from the normal in this respect, we could, with our present knowledge of cardiodynamics, determine the presence and estimate the extent of every cardiac abnormality except those specifically affecting the autonomic and conductive system.' We attempt to demonstrate enlargement by inspection and palpation. If, in adults, by either or both methods, we can demonstrate a true systolic heave to the precordium, we are justified in diagnosing at least some loss of myocardial reserve. If by percussion of the right and left cardiac borders we can be sure of an increase above the normal for that individual with respect to size, contour of thorax, etc., we have additional evidence of cardiac enlargement. If, under standard conditions, there is a definite preponderance of either ventricle in the electrocardiogram, or the fluoroscope, and if the orthodiascope or 6-foot roentgen-ray plate gives evidence of cardiac enlargement, we have even more positive evidence of loss of myocardial reserve. Here, again, one must

almost whole-heartedly agree with Eyster when he claims: "The most generally neglected of the aids to (cardiac) diagnosis is the roentgen-ray . . . We do not hesitate to carry out a comprehensive Roentgen-ray study of gastrointestinal cases, and yet the information generally obtained has usually a less direct bearing upon the underlying pathology than in heart disease."

More and more is the string galvanometer being given its proper evaluation. Certainly electrocardiographic tracings will never take the place of clinical findings, but when interpreted with the proper breadth of vision they are often invaluable in estimating the myocardial reserve. We must admit them to be the final court of appeal as to arrhythmias, and Levine[5,6] has shown that during operations the development of alarming cardiac symptoms usually has, as to the underlying factor, a sudden change in cardiac rhythm. Certainly the future holds more for electrocardiography as a help in determining the myocardial reserve, as is witnessed by the recent reports of Willius[7] on the high mortality and prognostic importance of all cardiac cases with what he calls "significant *T*-wave negativity."

To recapitulate, we have questioned one's ability to estimate the myocardial reserve upon: (1) *Certain subjective symptoms* without accompanying clinical and laboratory evidence; (2) *low systolic blood-pressure* and so-called *weak heart sounds;* (3) *systolic murmurs alone;* (4) a *poor reaction to effort alone* and (5) *certain arrhythmias* without further clinical evidence of myocardial changes. We have stressed the importance in estimating the myocardial reserve of: (1) A careful investigation for *infections, past and present,* possibly productive of damage to the myocardium; (2) a proper *association* of *subjective symptoms* with definite clinical and laboratory findings of *pathological changes;* (3) a proper interpretation of the so-called *reaction to effort;* (4) the importance in determining the *time* in the cardiac cycle at which *murmurs occur,* and the *character* rather than the intensity of the cardiac sounds; and (5), aided by careful inspection, palpation, percussion, roentgen-ray findings and conservative electrocardiographic interpretations, a *determination* of that which means more than any one single observation in estimating the amount of myocardial reserve, namely, *enlargement of the heart.*

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## DISCUSSION

Dr. Ross V. Patterson: I find little in Dr. Stroud's paper to discuss in the sense of diagreement from any of the statements therein contained. It would be difficult, of course, to exaggerate the importance of the myocardium in cardiac affections. The tendency of the last decade and a half has been to draw attention to the importance of that structure in increasing degree. MacKenzie was one of those who insisted upon a recognition of the importance of the myocardium, and due to his advocacy of that view, and also to others who held a similar view, we have gradually come to have more of a functional conception of cardiac affections and less of an antomical one. Anatomical conditions are today more appraised as of importance in affecting the ability of the myocardium to do its work. Valvular defects, pericardial adhesions, arterial thickening and hypertension, are chiefly of importance to the extent to which they impose upon the myocardium an additional burden which it may or may not be able to meet and at the same time adequately maintain the circulation. Changes in the heart muscle itself, in the mechanism of the cardiac contraction, and the influence of toxins are all to be regarded from the same standpoint. In a clinical appraisement of the condition of the heart functional capacity, as indicated by the reaction of the individual to effort, is often of more importance than an accurate determination of the anatomical conditions.

The problem in the management of most cardiac cases is maintenance of compensation, for the continuance of which we are chiefly dependent upon the inherent capacity of the myocardium. What we fear, of course, is heart failure, usually due to myocardial degeneration. At least the heart failure is largely contributed to by degeneration of the muscle. It is the expression of a disproportion between the power of the myocardium and the burden which it is called upon to bear. This disproportion may be occasioned by either a much weakened myocardium or an increase in the burden beyond its power.

The treatment of cardiac cases is usually the treatment of heart failure, an endeavor to improve either the condition of the myocardium or to

lessen the burden which it is called upon to bear, or to accomplish both of these objects. In other words, to relieve the disproportion.

A functional conception of cardiac disease has become general among those who have given special study to the subject. But it has not seemed to me that it is a view that has received as general acceptance as it should. When such a view becomes more general the management of cardiac cases will be on a much sounder basis.

Dr. George W. Norris: I feel that we are very much indebted to Dr. Stroud for setting forth lucidly and briefly a subject so large—a subject which in my judgment is extremely timely. It would have been timely five years ago, and probably will still be timely ten years hence, because of the notorious difficulty in getting the profession at large to accept new views. It is extremely difficult to eradicate from our minds the ideas we have been taught to accept as basic facts. As Dr. Stroud has said, it is high time that the medical profession should be very chary about ever using the term myocarditis. Undoubtedly there is such a thing. There are more or less definite types of it. We have one definite type in rheumatic fever, another in syphilis, another in septic diseases, another in hyperthyroid hearts and so on. In the vast majority of cases in which this diagnosis is made, the myocardium is not so much at fault as is some other factor. For instance, we see every year cases supposed to have heart disease because the heart is enlarged and a murmur is heard. They prove to be hyperthyroidism. We see a smaller but definite number which are supposed to have myocarditis because they are short of breath. Some of these have hypothyroidism and are cured by the administration of thyroid extract. One thought we might take away tonight, from what Dr. Stroud said: It would be just as well if none of us ever made a diagnosis of myocarditis as a finality. Let us put down myocarditis and then leave a blank to be filled in when we learn what the cause really is.

Dr. Stroud (closing): I have nothing much to add to the paper, but I would like to appeal for coöperation between the surgeon and the physician in this new heart work. We now have twenty-four heart clinics in Philadelphia. There are galvanometers in almost all the larger hospitals, and I feel that results will be more satisfactory for the physician and surgeon alike if we are asked to see cases before operation or in our heart clinics or by obstetricians in cases of early pregnancy, and urged to commit ourselves as to what we feel of the myocardial reserve in respect to possible operation or in respect to the pregnancy coming to term. I feel we should be in a position to give such opinions and that it is our duty to do so; but that the surgeons must coöperate with us in carrying out requests for electrocardiograms, fluoroscopic and $x$-rays examinations, and in the end both will mutually benefit.

# DIVERTICULA OF THE ESOPHAGUS; PULSION, TRACTION, MALIGNANT AND CONGENITAL*

By CHEVALIER JACKSON, M.D., Sc.D.

AND

THOMAS A. SHALLOW, M.D.

## Esophagoscopic Observations

BY CHEVALIER JACKSON

Incoördination of the Cricopharyngeal Pinchcock as an Etiologic Factor in Pulsion Diverticulum.—The cricopharyngeus muscle is in my opinion an important factor in the etiology of pulsion diverticulum (Figs. 1 and 2). These orbicular fibers of the inferior constrictor merge with the circular fibers of the esophagus. Some anatomists seem to regard them as part of the inferior constrictor and other anatomists seem to regard them as circular fibers of the esophagus. To the esophagoscopist, however, the living active muscle looms in huge proportions because, so long as it remains contracted, it acts as an impassable barrier to the safe passage of the esophagoscope. Making gentle pressure with the tube-mouth, he waits patiently until the cricopharyngeus relaxes sufficiently to allow the esophagoscope to enter the esophagus. No one who examines this region on the cadaver has any conception of the bone-like hardness of the mucosa-covered cricopharyngeus when contracted in a patient who is not under general anesthesia. This hardness led early esophagoscopists to think it was the cricoid cartilage that was encountered. The author, however, demonstrated[1] that the resistance was on the posterior wall and was due to the orbicular muscular fibers (Fig. 2) that are essentially different in power and action from either the circular fibers of the esophagus on the one hand and from the oblique fibers of the inferior constrictor

* Read February 4, 1925.

on the other. To the author, looking through the esophagoscope, it is obvious that the oblique fibers remain contracted while the orbicular fibers relax. This constitutes a separate action with

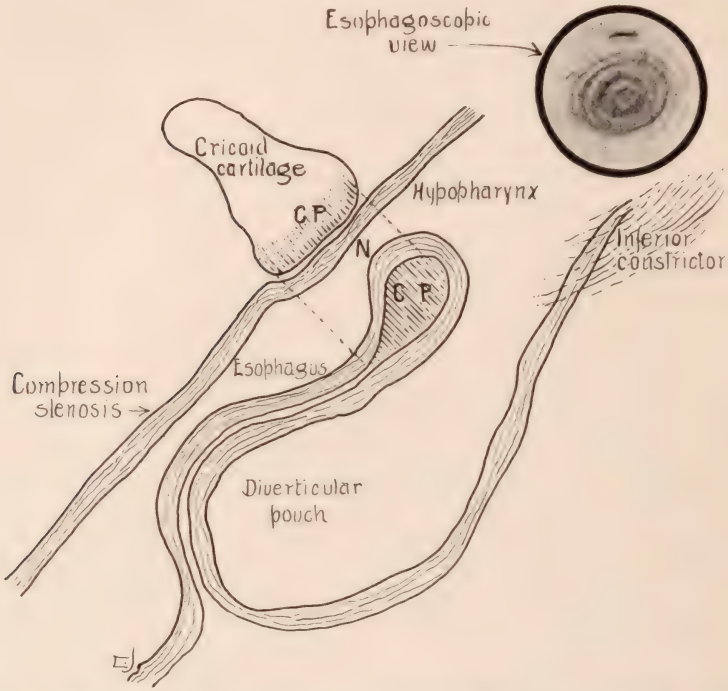


FIG. 1.—Schema showing the authors' theory of the *functional* factor in the etiology of pulsion diverticulum. The chief functional etiologic factor is the cricopharyngeus muscle *CP*, which normally pulls the cricoid cartilage back against the spine, maintaining, in health, a tonic closure of the esophageal mouth *N*. The abnormal etiologic factor arises when the cricopharyngeus fails to relax at the approach of the bolus propelled by the powerful contraction of the inferior constrictor, the powerful squeezing muscle. The *structural* factors demonstrated by Mosher are doubtless of equal or greater importance. This drawing also illustrates the secondary compression stenosis, which, along with the enlargement of the pouch and the increased deglutitory pressure, constitutes the vicious circle on which inevitable increase of dysphagia and discomfort depends. In the esophagoscopic view, the cricopharyngeus muscle *CP*, is concealed under the mucosa between the diverticular pouch shown below and the slitlike orifice of the subdiverticular esophagus shown at the top of the circular field of vision.

distinct innervation that entitles this group of muscular fibers to a separate name. The separate name serves well the study of the mechanism of deglutition and of the technic of introduction of the

esophagoscope. Passing on down with the esophagoscope, nothing similar to the cricopharyngeal constriction is found throughout the entire length of the thoracic esophagus. It is, therefore, clear that there is something more powerful at the cricopharyngeal level than in the esophageal wall. It is not until the hiatus esophageus is reached that we encounter a like rigidity. At this point we have another group of periesophageal muscles, the diaphragmatic pinchcock musculature of the diaphragm.

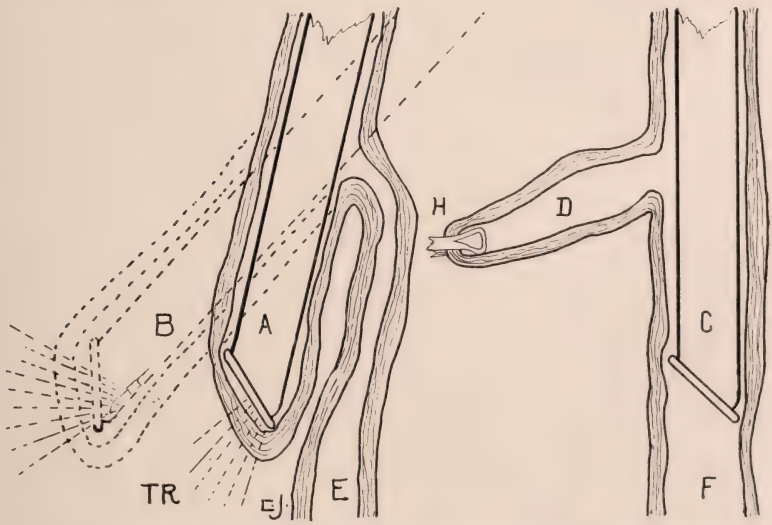


FIG. 2.—Schematic representation of esophagoscopic aid in the excision of a diverticulum. At *A* the esophagoscope is represented in the bottom of the pouch after the surgon has cut down to where he can feel the esophagoscope. Transillumination (*TR*) from the esophagoscopic lamp greatly assists the surgeon in identification and dissection. Then the esophagoscopist causes the pouch to protrude, as shown by the dotted line at *B*. After the surgeon has dissected the sac entirely loose from its surroundings, traction is made upon the sac, as shown at *H*, and the esophagoscope is inserted down the lumen of the esophagus, as shown at *C*. The esophagoscope now occupies the lumen which the patient will need for swallowing. It only remains for the surgeon to remove the redundancy, without risk of removing any of the normal wall. This is known as the Gaub-Jackson operation.

Whatever may be the anatomists viewpoint, he who does esophagoscopy without anesthesia cannot but feel that it is wrong to class the orbicular fibers at the upper end of the esophagus as simply part of the circular coat of muscles of the esophagus, on the one hand, or simply part of inferior constrictor on the other.

It is my opinion, based on esophagoscopic studies, that *it is the*

*barrier presented to the advance of the bolus by the unrelaxed cricopharyngeus that is the functional factor that herniates the pharyngeal wall, thus creating the pharyngeal diverticulum.* The wall of the hypopharynx and esophagus is weak everywhere, but

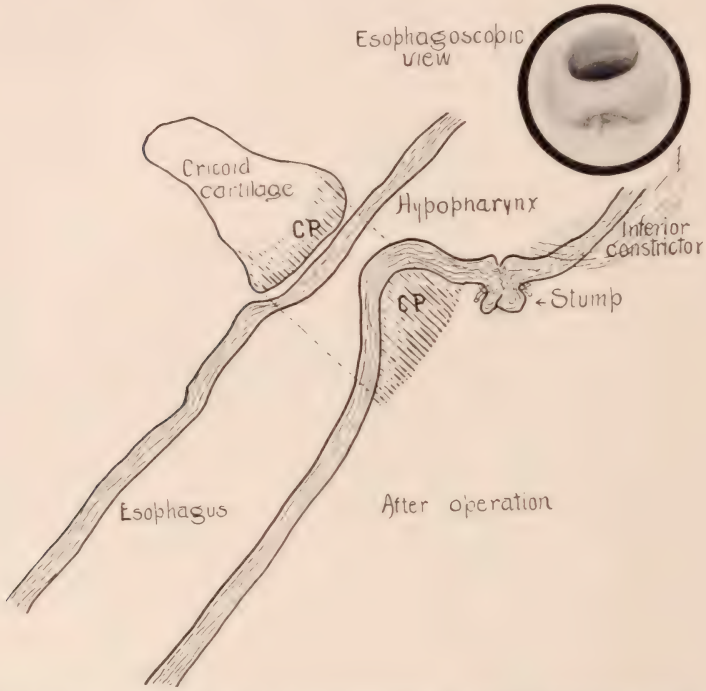


FIG. 3.—Schematic illustration of postoperative conditions elucidating further the functional factor in the primary etiology and illustrating the advisability of esophagoscopic stretching of the cricopharyngeus muscle, *CP*. The inferior constrictor, the powerful squeezing muscle, propels the bolus in the direction of the subdiverticular passage *N*, surrounded by the cricopharyngeus muscle *CP*, to reach the esophagus. If the cricopharyngeus fails to open promptly, widely and coördinately, enormous pressure is put upon the stump of the removed diverticulum, causing in some cases leakage before and recurrence after healing. Overactivity of the cricopharyngeus is obviated by careful esophagoscopic stretching at operation. In addition to the incoördination referred to, the structural factors demonstrated by Mosher contribute to the primary etiology. The drawing shows the stump before final inversion.

is as strong here as elsewhere, and seems better supported in the neck than in the case of the thoracic esophagus. But the thoracic esophagus does not have the obstruction ahead except in cases of so-called cardiospasm, which is due, in many cases at least, to failure

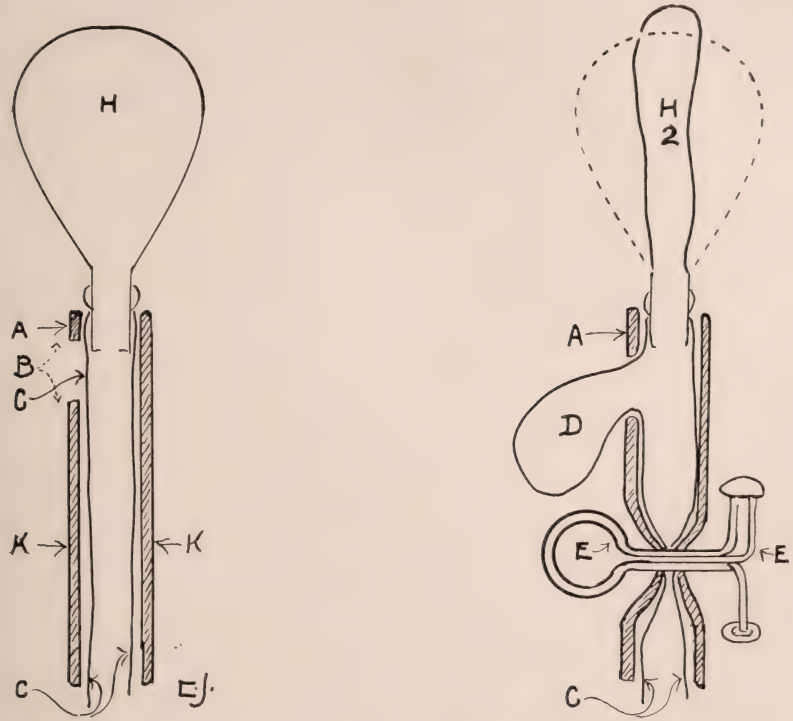


FIG. 4.—Schematic sketch of the working model used by the author at the Graduate School of Medicine, University of Pennsylvania, to demonstrate incoördination of the cricopharyngeal pinchcock as the functional factor in the etiology of pharyngeal diverticulum. At *H* is shown a hand-bulb representing the inferior constrictor, or squeezing muscle. To it is attached the Penrose tubing *c*, *c*, which represents the relatively thin, elastic wall of the pharynx and esophagus. The heavy-walled tubing *A*, represents the tissues that normally support the thin elastic esophagus, the anatomical weak place in this support being represented by the hole in the heavy tubing at *B*. This hole is closed only by the unsupported thin Penrose tubing, *C*. To represent the cricopharyngeal muscle, at *K*, *K*, is located one of the ordinary laboratory pinchcocks used on the tubing of burettes, etc., for stopcocks; but this pinchcock is not shown at *K* in order better to convey the idea of the widely open condition present at the moment of normal swallowing. At this moment in the normal deglutitory cycle the inferior constrictor (represented by *H*2) contracts on the bolus, squeezing the latter downward; simultaneously the cricopharyngeus (at *K*, *K*) which is at all other times tonically contracted, coördinately opens widely, so as to offer little or no resistance to the approaching bolus. If, however, instead of coördinately opening widely, as at *K*, *K*, the cricopharyngeal pinchcock (represented at *E*, *E*) as the result of incoördination, remains tonically closed tightly an enormously increased pressure is put upon the hypopharyngeal wall. The well-supported portions withstand the pressure, but the anatomically and atavistically weak point in the support, *B*, results in the herniation of the normally thin and elastic cricopharyngeal wall, *C*, resulting gradually in the ultimate development of the pouch *D*.

of the diaphragmatic pinchcock muscles to relax; in other words, a pathologic mechanism analogous to that present in pharyngeal diverticulum. Summing up the matter, the essential mechanism is not so much the propulsion of the oblique fibers of the inferior constrictor, as the failure in the coördinate obliteration of the normal obstruction ahead (Fig. 4).

FIG. 4*a*.—Schematic illustration of classic type of traction diverticulum due, or supposed to be due, to traction of a scar external to the esophageal wall at *A*. It has been supposed that the reason such diverticula are symptomless is that the lower rim of the pouch *B* is as low as the bottom of the sac or at least lower than the upper rim of the entrance to the pouch *E*. In the authors' opinion, however, the true reason lies in the anatomical fact of the absence of an orbicular muscle at *D* to act analogously to the cricopharyngeus, which in the authors' opinion is a powerful factor in the etiology of pulsion diverticula.

Normal salivary drainage when no food or drink are being taken is a mere leakage through the opposed mucosal surfaces at the cricopharyngeal and diaphragmatic pinchcocks, and this leakage is sufficient ordinarily to prevent drooling without active deglutition. Any excess of saliva, however, as for instance at the thought of eating oranges, will cause swallowing to open the pinchcocks to let the excess saliva through, and thus to prevent drooling.

In a number of our cases of pulsion diverticulum organic stricture in the orifice has required esophagoscopic dilatation. Because of the coördinate failure of the cricopharyngeal pinchcock to open,

seeming an important factor in etiology, it has seemed to us advisable to stretch the cricopharyngeal constriction gently even when not organically strictured, to lessen the tendency to recurrence. This cannot be done with the same vigor as in the case of the anal spincter at a hemorrhoidal operation. The passage of the largest-sized esophagoscope is usually sufficient and is safe in careful experienced hands. This has, we believe, been an important factor in the prevention of postoperative leakage and in prevention of recurrence of pulsion diverticulum, in our cases.

The mechanism of so-called traction diverticulum is essentially different (Fig. 4*a*).

## Esophageal Diverticula from the Surgeon's Viewpoint

BY THOMAS A. SHALLOW, M.D.

Diverticula of the esophagus are not increasing in frequency, but the diagnosis is now made much more certainly than formerly. Diverticula used to be missed, they are now discovered. The improved methods of diagnosis, the esophagoscope, the fluoroscope and roentgenograms, enable us to recognize this operable form of dysphagia and to distinguish it with certainty from other often inoperable forms. Hence diverticula are now more frequently recognized.

In contrast with the certainty of present-day diagnosis, the older literature shows many cases in which the cause of the dysphagia was never recognized during life and in which a postmortem examination disclosed a pulsion diverticulum.

Much has been said of the etiology and of the morphological characteristics of esophageal diverticula. Two types of diverticulum of the esophagus are accepted by authors, viz.: (*a*) The pulsion type; (*b*) the traction type.

We desire to set forth in this paper several unusual forms of diverticula: (1) The congenital form; (2) the double diverticula; (3) a form in which malignancy is a contributing cause. We will question the accepted view—that diverticula do not occur before middle life and will present a case in which symptoms of a diverticulum existed in a boy aged twelve years.

Congenital Diverticula. In presenting a case which we believe to be one of congenital diverticulum, we realize that William

Boyd[2] states that congenital diverticula do not exist. If this view of Boyd's is correct, then, of course, we are wrong and we must try to determine with what we are dealing. Is it a traction diverticulum or is it the hypertrophied remains of one of the branchial clefts? With these thoughts in mind we present the case.

Case I.—J. B., male, aged eight years, was admitted to the surgical service of Prof. J. Chalmers Da Costa, with fever, flatness of the right side of chest and all the physical signs of empyema. Following a rib-resection for the evacuation of pus, which was present, he discharged particles of food through the external chest wound. Because of his very poor condition and the necessity of a gastrostomy, which was done, esophagoscopy was delayed until the symptoms of sepsis subsided. The patient died fourteen days after the operation without diagnostic esophagoscopy and the clinical diagnosis of perforation of the esophagus was made. Postmortem examination by Dr. Baxter L. Crawford disclosed a narrow tube springing from the posterolateral wall of the esophagus, 11 cm. from the laryngeal opening, extending downward and backward. The tube was 2½ cm. long, 4 cm. in diameter, and of equal caliber throughout its entire length. The course of the tube was downward and outward. The distal end opened into the chest cavity through the dome of the pleura, thus explaining the cause of the empyema and the reason for the food passing through the thoracotomy wound. Microscopic examination of this tube showed its wall to be in three distinct layers, corresponding structurally to those of the esophagus, and hence our decision that the tube was a true diverticulum (Fig. 1). Sections made at various levels of the tube showed the same distinct layer arrangement of mucosa, submucosa and muscular fibers. This fact, in conjunction with the almost right-angle connection of the tube with the esophagus and the absence of any inflammatory changes in the esophageal wall or near the junction of the tube to the esophagus, led us to discard the diagnosis of traction diverticulum. To account for this unusual condition we, therefore, should consider the possibility of a pharynegal branchial fistula as a causative factor.

Maylard[3] states that a congenital diverticulum may be caused by the persistence of one of the branchial clefts. We are told by von Bergmann[4] that a persistent branchial cleft, with the resultant cyst or fistula, involves the second cleft only, the course of the cyst or fistula being between the internal and the external carotid arteries. The internal landmark of a second branchial cleft is in the pharynx behind the tonsil, at which point the fistula may open into the pharynx. If an external fistula is present, the cutaneous opening is along the anterior edge of the sternocleidomastoid muscle. Thompson[5] states that internal openings due to perforation of the

third or fourth cleft membranes are infrequently seen, but when present they open lower down in the sinus pyriformis. He further states that the course of the tract of the third cleft is below the internal carotid artery and above the superior laryngeal nerve. The same author says that theoretically a fourth cleft should pass downward; on the right side it should hook around the subclavian artery and on the left side it should hook around the aorta. Thompson remarks, in his article, that he is not familiar with any observation showing a fistulous tract passing around the subclavian artery or the aorta. Let us compare the morphology of the wall of a fistula of the second branchial cleft as found in the case of Seelaus[6] with the following report of Dr. Crawford in our case of congenital diverticulum:

Specimen consists of a small, tubular structure measuring 6 cm. in length. The average diameter is 0.75 cm. At one extremity there is a small pinpoint opening and on cross-section there is a lumen throughout the length of the specimen with average diameter of 0.5 cm. The lumen, however, is much smaller in some places than in others. Formalin fixation.

*Histology.* On cross-section the structure is found to possess a definite lumen which is lined with stratified squamous epithelium and just beneath this epithelial lining in places there are collections of lymphoid tissue and also a few mucous glands are observed. There is a definite fibrous tissue coat forming the main portion of the wall of the fistula, but no muscle is observed except fragments of striated muscle attached externally. The mucosa is inflamed and ulcerated and in places the lumen is filled with necrotic material and leukocytes, many of which are polynuclears. Sections were taken from various portions of the structure and the epithelial lining is constant. Microscopic examination of cross-section showed same to be lined with stratified squamous epithelium and a thickened submucosa. The muscular coat is well developed (Fig. 5).

*Diagnosis.* Squamous epithelial-lined fistula.

From what has been said by Thompson and von Bergmann, the depression of the second cleft is behind the tonsil. This point is far above the site of the origin of the congenital diverticulum described in this paper. It necessarily follows that the tube we describe as a congenital diverticulum does not spring from the second cleft. There are no recorded cases of fistula of the third or fourth clefts to compare with the structure found in our case. It is also noted that the opening into the esophagus in our case is far below the point where Thompson states the third and fourth clefts should

open. We, therefore, assume that we are dealing with a true congenital diverticulum.

FIG. 5.—Photomicrograph of cross-section of congenital diverticulum existing in a boy eight years of age, showing the distinct mucous coat and part of the muscular coats. The entire specimen is of the same caliber throughout.

JUVENILE DIVERTICULA. The common view that diverticulum of the esophagus does not exist before the fortieth year is shaken by the following case:

CASE II.—Dr. D. W., male, aged fifty-four years. Dr. W. stated that when a youngster on a farm he amused the other boys by regurgitating grapes which he had swallowed a number of hours before. During the period of forty years from the time he came to operation he had the classical symptoms of diverticulum of the esophagus, with the exception that he did not begin to lose weight until very recently. He accounted for this by the fact that after filling the sac with food he was able to swallow without difficulty. *X*-ray examination by Dr. Manges disclosed an esophageal

diverticulum at the pharyngo-esophageal level. The sac is a little to the right in the median line and almost entirely on the posterior wall. Fig. 6 will show the size and location of the sac.

FIG. 6.—*Juvenile diverticulum.* Present symptomatically for forty years prior to operation. The symptoms were first noticed when patient was twelve years of age by his trick of voluntarily regurgitating grapes which he had eaten a number of hours before.

This unusual history obtained from a physician practising in one of the large cities of New York State leads us to believe that diverticulum of the esophagus may exist in some cases long before the fortieth year and because of the trivial symptoms manifested remain undiagnosed for years. Therefore, in order to emphasize the possibility of early origin, we have classified this case as a juvenile diverticulum.

Double Diverticula. Great emphasis has been placed by various writers on diverticulum of the esophagus on the supposed causative factor. They all agree that there is a congenital weakness at Lannier's triangle. This congenital weakness should be regarded

Fig. 7.—*Double diverticulum.* Showing one pouch filled and the other pouch filling. Prior to operation this patient was able to return two full glasses of water. It will be noticed in this picture that one pouch presents on the left side and the other pouch on the right side. Esophagoscopy revealed two sacs with two separate openings.

as being at least a part factor in the production of diverticula. That some other factor or factors are concerned in the production of diverticula is unquestionably true, otherwise multiple diverticula could not form. In the case we are now presenting we show by the

*x*-ray picture a double diverticulum. We present a second plate to show the second diverticulum existing after the removal of the first (Figs. 7 and 8). The *x*-ray findings were confirmed by esophagoscopy.

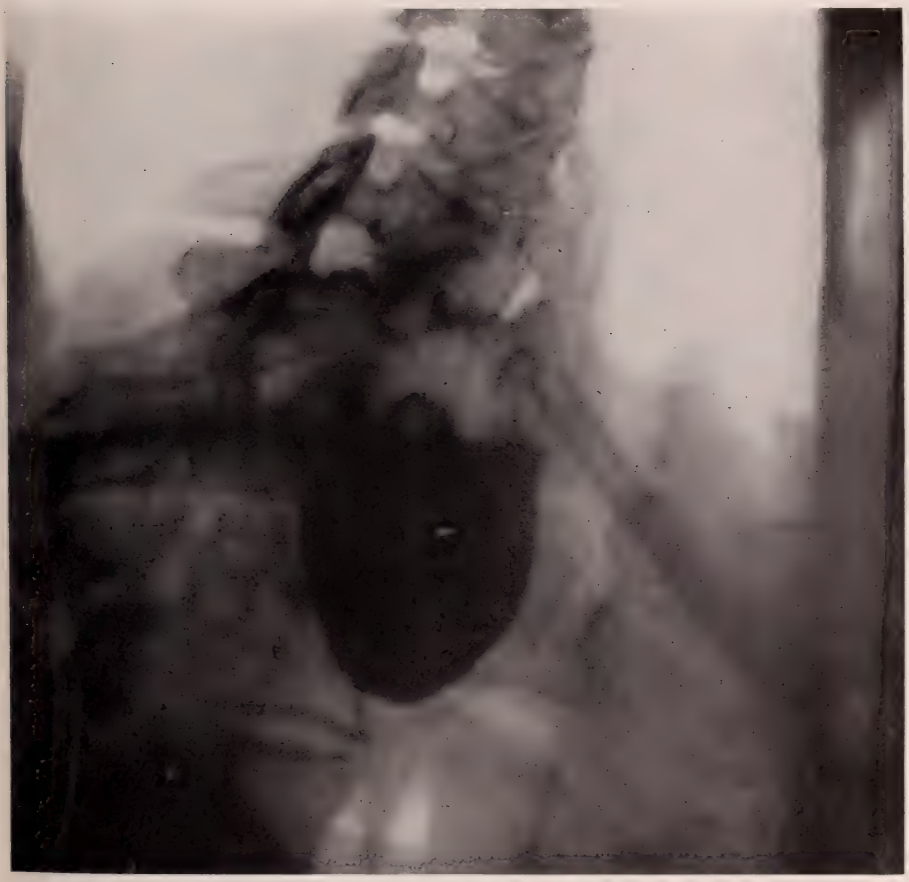

FIG. 8.—*Double diverticulum.* Showing the left pouch remaining after the removal of the right pouch, as shown to exist in Fig. 7.

CASE III.—P. B., male, aged sixty-five years. The chief complaints are difficulty in swallowing and the loss of 60 pounds in weight. The present illness dates back twenty years, at which time the patient first noticed that he was able to regurgitate food that he had eaten some hours before. He fixed this date absolutely in his mind because he moved from one part of Pennsylvania to another at this period, which he states was twenty years ago. During the past three years he noticed increasing

difficulty in swallowing food and a peculiar noise in his throat when eating, so that he was compelled to eat alone. He was treated by many physicians for various conditions. A diagnosis of diverticulum was made. *X*-ray examination by Dr. Manges shows "quite a large diverticulum of the esophagus, which has two distinct pouches; the smaller one, and the higher, extends toward the left, and the larger one is more nearly in the median line, presenting toward the right posteriorly."

*Operation.* Preliminary gastrostomy was performed under local anesthesia. After an interval of ten days he was operated upon by the combined method. The diverticulum presenting on the left side was exposed and found to extend down to the suprasternal notch. The capacity of this sac was 6 ounces. The esophagoscopic examination by Dr. Jackson during the course of this operation disclosed two openings, one above the other, with no communication between the sacs. In other words, it was not a multilocular single diverticulum, but each sac sprang from an independent site. Figure 8 shows the remaining diverticulum after removal of the first. Ten days following the removal of the first diverticulum the right side was operated upon by the combined method. The fundus of the diverticulum was adherent to the dome of the pleura and to the subclavian vein. The neck of the sac seemed to expand as it approached the esophagus. A glance at the first plate, showing the presence of both diverticula, will give you an idea of the broad barium surface present in the picture. The sac was amputated close to the esophagus. The procedure was a one-stage operation.

The patient reacted from the operation; but to our chagrin, a number of months later, he returned with a history that he was again storing up food and had developed the symptoms of a diverticulum. The *x*-ray plate disclosed that he had a diverticulum on the right side which extended into the chest cavity, and was probably a recurrence and not a sac missed at the former operation. He was again operated upon by the combined method and it was found by Dr. Jackson that the opening was toward the right, probably in the region of the original right-sided diverticulum. In exposing the fundus of the diverticulum in the chest cavity, and in order to protect the innominate and subclavian vessels, it was necessary to use in the root of the neck an abdominal retractor with a $2\frac{1}{2}$ inch blade. It was found that the fundus of the sac was adherent to the arch of the aorta, from which structure it had to be cut by long-handled gynecological scissors. The parts were illuminated by the light of an additional bronchoscope passed along the retractors in the root of the neck, thus direct vision could be employed. The sac was amputated at its junction with the esophagus. It was a one-stage operation. The mediastinum was protected by iodoform gauze and a small cello-silk drain was introduced.

There was much more reaction from this operation than from any of his previous ones. He was fed through a Rehfuss tube by way of the nose for eighteen days, at the expiration of which time the tube was removed. The patient is now swallowing without any difficulty, six months after the operation, and we hope that a permanent cure has been obtained.

Malignancy as a Cause of Traction Diverticulum. To consider the 2 previous cases, one of which existed for forty years and the other for twenty years, is to wonder why malignancy does not occur in diverticula more frequently than has been reported. In presenting this case we do not wish to give the impression that we are dealing with a pulsion diverticulum which had undergone malignant changes, but to show that if the sac preceded malignant growth that it was a traction diverticulum, and also to point out the uncertainty of even *x*-ray diagnosis and the necessity for esophagoscopy. The case is presented in this series to emphasize the absolute necessity of esophagoscopic study previous to any operation of this nature on the esophagus. The results of the esophagoscopic examination were absolutely conclusive. The specimen removed for study disclosed a squamous-cell epithelioma.

Case IV.—J. T., male, aged sixty years. The chief complaints are difficulty in swallowing solid food, loss of weight, intermittent pains across the sternum and slight hoarseness. The present illness dates back only eight weeks, at which time the patient first noticed difficulty in swallowing solid food. With the onset of this condition he began to regurgitate food. The *x*-ray examination was made by Dr. Manges: "There is an organic lesion on the upper end of the esophagus at the level of the suprasternal notch, a little lower than the usual site of a diverticulum, but there is apparently a diverticulum present. The lower border is irregular. I suspect there are adhesions. We believe it is a diverticulum, but we are unable to exclude a possible infiltrating growth" (Fig. 9).

The results of the esophagoscopic examination and the laboratory report of the specimen influenced Dr. Jackson to advise a preliminary gastrostomy and the removal of the upper part of the esophagus, including removal of the diverticulum.

Under intratracheal ether anesthesia the esophagoscope was introduced so that it passed below the level of the growth. A collar incision was made in the neck, the recurrent laryngeal nerve of the left side was isolated and drawn outward. The left lobe of the thyroid gland was removed and the esophagus was exposed. At the suprasternal notch the esophagus was found to be densely adherent to the fascia at the fundus of the diverticulum. I believe it to have been a traction diverticulum, and I believe so because of the dense adhesions surrounding the esophagus at this point. With the esophagoscope in position in the esophagus, we exposed the normal esophagus 2 inches below the suprasternal notch. The esophagoscope was then withdrawn, the esophagus was ligated, was severed below the growth and the distal end was invaginated. The upper portion of the esophagus was removed to its origin. At this point it was ligated, but it was impossible to get a perfect invagination.

Iodoform gauze was used to protect the mediastinum from any leakage

from the upper end of the pharynx. The patient reacted well from the anesthetic and made an uneventful recovery. It is now a number of months since the operation and as yet he shows no sign of local recurrence of the growth. He has gained in weight and is being fed through a gastrostomy opening.

We believe that the carcinoma caused a traction diverticulum.

FIG. 9.—*Malignant diverticulum.* Showing the existence of a diverticulum which showed malignancy. A distinct pouch with irregularities in its base. It will be observed that this pouch is much lower than the pulsion diverticulum. Pouch with the esophagus extirpated. This was not merely a case of dilatation above a malignant stricture.

PULSION DIVERTICULA. Our experience with pulsion diverticula leads us to say that they do not all spring from the one narrow location usually assigned to them. Some are lower than others. We have noticed that they may arise irregularly in an area about ½ inch

below the junction of the pharynx and the esophagus. von Bergmann calls sacs arising at this low level deep esophageal diverticula.[7]

FIG. 10.—*Traction diverticulum.* Showing the existence of a cervical traction diverticulum which was not extirpated but anchored to the deep cervical fascia.

The pouch originates on the posterior aspect of the esophagus and usually advances toward the left or right, usually to the left, and gradually increases in size. With the increase in size the esophagus may be drawn upon and partially rotated on its longitudinal axis. When rotation arises, swallowing becomes more difficult and the diverticulum increases more rapidly in size. May not rotation

of the esophagus account for the variation in the size of the diverticulum in different patients? That the sac does not develop toward the left side of the neck in all cases is exemplified by several of our patients. In these the sac was found on the right side of the neck. This fact is of some importance from a surgical standpoint. The operation should be done on the side of the neck on which the sac presents, because with the rotation of the esophagus toward the side on which the sac is more pronounced, one is able to obtain a better exposure for repairing the opening in the tube.

Complications. Complications of the operation for pulsion diverticulum of the esophagus are: (1) Insufflation pneumonia, caused by manipulating a partially-filled sac and squeezing out semiputrid contents; many septic particles are inhaled from large diverticula. (2) Mediastinitis, due either to primary soiling of the wound in manipulating the sac or to leakage from the site of the amputation of the sac during convalescence. (3) Secondary hemorrhage from one of the thyroid arteries exterior to the thyroid gland or from vessels of the gland itself. (4) Esophageal fistula may follow an operation, or a sac may reform. (5) Recurrence of the diverticulum.

*Operation.* We believe the employment of the esophagoscope as an aid to the surgeon simplifies the operation to such an extent that the use of this instrument is almost indispensable (Fig. 2). The esophagoscope, by transillumination of the sac and by lifting it from its bed, permits the operator to pick it up quickly. The sac is emptied by aspiration through the esophagoscope, and foreign material, such as foreign bodies (in one case there were pieces of an oyster shell) and retained food and secretions, are removed. By this procedure the danger of aspiration pneumonia is practically eliminated. This method of operation is known as the Gaub-Jackson[8] operation (Fig. 2).

After the delivery of the sac the esophagus is examined at intervals by the esophagoscope in order to detect the presence of any deformity of the gullet below the diverticulum. It is sometimes noticed that there is a constriction below the diverticular opening. If found, this stenosis must be treated by the surgeon during the suturing of the esophagus. Finally, in reinforcing the esophageal walls by sutures, the danger of causing too much narrowing of the esophagus is prevented by the esophagoscope being left in position, within the lumen of the esophagus, until suturing has been completed (Fig. 2).

The danger of infection during operation is to a great extent eliminated by the thorough emptying of the sac through the esophagoscope, so that when the amputation of the sac is performed there is little danger of contamination. The danger of the development during convalescence of infection, from the site of closure of the neck of the diverticulum, formerly gave us a very great concern, so much so that it was our habit to employ preliminary gastrostomy for feeding during this period. We have abandoned this precaution and feed all of our patients through a Rehfuss tube left in position through the nose and in the stomach during the entire convalescence. This suggestion was made by Dr. F. O. Lewis and Dr. Louis H. Clerf.

In this series of cases we have used in some the one-stage operation and in others the two-stage operation with fixation of the sac. As the result of our experience we believe that the one-stage operation, with the aid of the esophagoscope and with the use of the Rehfuss tube, is the safest and gives the best results.

*Technic of Operation.* Under intratracheal ether anesthesia the patient is prepared in the usual manner and an incision is made on the side of which the sac presents and along the anterior border of the sterno-cleido-mastoid muscle. It is to reach from the level of the hyoid bone to 1 inch above the sternum and is to pass through the skin and deep fascia, exposing the anterior belly of the omohyoid muscle. This muscle is then to be divided transversely. In this cut the external jugular vein may be exposed and, if it is, it should be divided and tied. The common carotid artery and the internal jugular vein are now exposed and retracted outward. If the thyroid gland is decidedly enlarged it is sometimes necessary to ligate and cut the superior thyroid artery. The trachea and the esophagus will be found to be encased in a common sheath, which is to be incised, exposing the esophagus in the posterior part of the wound and the trachea in the front. The trachea is then retracted toward the midline.

The esophagoscope is introduced by Dr. Jackson or one of his associates, Dr. Louis H. Clerf or Dr. Gabriel Tucker. The sac is emptied of its contents by aspiration, thereby avoiding squeezing the fluid into the pharynx. The esophagoscope is then introduced into the bottom of the diverticulum, the sac transilluminated and the esophagoscopist rotates the sac into the wound. The sac is grasped with the Babcock clamps and drawn further upward and

outward. It will be found at this point that the sac is sometimes covered by a thin layer of muscle. This muscle is separated. The sac is then freed to the junction of the diverticulum with the esophagus, being careful to free all muscle fiber from its covering. The neck of even the largest diverticulum is seldom ½ inch in diameter. A neck apparently larger than this usually means incomplete dissection, the genuine neck not having been reached. The sac is then transfixed with a small intestinal needle carrying No. 1 iodized catgut in much the same way as a hernia sac is transfixed, and is severed close to the esophagus. By this method no leakage occurs during section.

We believe that the mere amputation and ligation of the sac without preliminary transfixion and ligation are not sufficient to cure a diverticulum of the esophagus. After transfixion, ligation and amputation we reef the area of gullet around the base of the stump by the use of three sutures of catgut, inserted at intervals, each one picking up the muscular coat of the esophagus. These stitches cause inversion. Some surgeons use a purse-string stitch, but if the opening is large it is impossible to cover the stump by this method. Simple reef stitches at several points of the circle invaginate the stump easily and firmly. By leaving the ends of the reef stitches long enough the suture line can be reinforced by the ends carried across and tied to the opposite ends. This narrows the esophagus to a certain extent and if the esophagoscope was not *in situ* during the suturing the danger of narrowing would be decided. The musculature upon the sac which was separated in freeing that structure is then sutured with No. 1 gut over the embedded stump, not so much to secure strength, but to give an additional protection against leakage during the first few days. The incision in the neck is closed in layers, no drainage being used except a small piece of cello-silk placed beneath the deep fascia.

We do not use tube drainage or gauze drainage. A rubber tube may make pressure on the thyroid gland and also be responsible for secondary hemorrhage. This is especially apt to be the case if the patient is restless or has severe spells of coughing. A great many of the cases we operated upon for esophageal diverticulum had chronic bronchitis before the operation and during the postoperative period coughed up a considerable quantity of mucopurulent matter. One of our patients developed secondary hemorrhage from this cause. We believe that gauze tends to produce leaking and a

fistula in the same way as it does after an operation for vesico-vaginal fistula or suturing the ureter.

## Case Reports

Case I.—J. B., male, aged eight years. This case was discussed in the general text of this paper as a congenital diverticulum.

Case II.—D. W., male, aged fifty-four years. This case was discussed in the general text under juvenile diverticulum.

Case III.—F. B., male, aged sixty-five years. This case was discussed in the general text of this paper as a multiple diverticulum.

Case IV.—J. T., male, aged sixty years. This case was discussed in the general text of this paper as a malignant traction diverticulum.

Case V.—H. E., male, aged sixty-eight years. Chief complaint: Difficulty in swallowing any dry, solid food. This condition has existed for the past year and within the past few months has become more pronounced. He is conscious of gurgling noises in the throat, particularly after eating. There is nothing in the family or personal history that could bear upon his case except that he had typhoid fever fourteen years ago. He has lost considerable weight, the exact amount he is unable to determine. Esophagoscopic and *x*-ray examinations were made by Dr. Jackson and Dr. Manges. Dr. Manges says there is a small diverticulum of the esophagus at the level of the seventh cervical vertebra on the posterior wall in the median line.

*Operation.* No preliminary gastrostomy was done, but the combined esophageal operation by Dr. Jackson and Dr. Shallow disclosed a small sac. Because of the patient's general condition it was deemed advisable not to amputate the sac at the preliminary operation, but to leave it for a secondary operation. The sac was, therefore, freed and surrounded by gauze. On the eighth day the sac sloughed and left a discharging sinus. This fistula discharged for a number of weeks, but finally closed without any secondary operative intervention.

*Postoperative Progress.* The patient remained in the hospital three weeks after the operation. The fistulous tract had not entirely healed on discharge, but was healing rapidly. He was seen the following month and the neck was entirely healed. There has been no further trouble with this diverticulum.

Case VI.—F. D. P., male, aged fifty-six years. Chief complaints: Lodgment of food in the neck and noisy deglutition. The first intimation that the patient had as to any obstruction in his esophagus was, two years ago, when he spat out a watermelon seed he had eaten a number of hours before. *X*-ray examination by Dr. Manges discloses a diverticulum of the esophagus, perhaps a little to the left of the median line. It has rather

a narrow opening and the sac holds about ½ ounce. Esophagoscopic examination by Dr. Jackson confirms the *x*-ray diagnosis as to the size and location.

*Operation.* No preliminary gastrostomy. The combined Gaub-Jackson operation by Dr. Clerf and Dr. Shallow. Primary amputation of the sac, reinforcement of the esophagus. Closure except for small piece of cello-silk beneath the deep fascia.

*Postoperative Treatment.* The patient was fed through the nose by means of a Rehfuss tube passed into the stomach and retained for eighteen days. Stitches and cello-silk removed on the tenth day. Primary healing of the wound. *X*-ray examination on the sixteenth day, by Dr. Manges, disclosed no evidence of diverticulum, but a slight narrowing of the esophagus at the site of the original opening of the sac.

Case VII.—Mrs. E. D., female, aged sixty-two years. Chief complaint: Regurgitation of particles of food several hours after eating. Clicking sensation on swallowing. Trouble has existed for past five years. She has been treated by numerous physicians for "nervousness." She has lost about twenty pounds. *X*-ray examination, by Dr. Manges, disclosed a rather large diverticulum of the esophagus a little higher than the average, apparently just a little below the larynx. Esophagoscopic examination, by Dr. Jackson, disclosed an opening about in the site shown by the *x*-ray.

*Operation.* Combined Gaub-Jackson two-stage operation. The sac was found to be large and at outer surface adherent to the right side of the neck. The outer surface was composed of muscle which had much the appearance of the constrictors of the pharynx. Owing to the large size it was deemed advisable to do a two-stage operation. The sac was surrounded by gauze (iodoform) and the wound was left open. On the tenth day secondary operation was done with closure of the opening, which was on the lateral wall of the pharynx.

*Postoperative Treatment.* Patient was fed through a Rehfuss tube, as was Case VI, for eighteen days after the completion of the second operation. *X*-ray examination following the second operation did not disclose any evidence that a diverticulum had ever existed.

Case VIII.—L. R., male, aged forty-seven years. Chief complaints: Difficulty in swallowing solid food, regurgitation of food and noisy deglutition. *X*-ray examination disclosed a moderate-sized diverticulum of the esophagus at the usual location. The sac is very little more than an inch in diameter.

*Operation.* Combined Gaub-Jackson method, by Dr. Jackson and Dr. Shallow. The sac was exposed and found to spring from the posterior wall of the esophagus. The sac was amputated, the wound in the esophagus was ligated and sutured as directed and the incision was closed except for a cello-silk drain.

*Postoperative Treatment.* Drain and stitches were removed on the tenth day. During the convalescence the patient was fed through a Rehfuss tube for sixteen days. *X*-ray examination following the operation: "There

is no indication that a diverticulum of the esophagus ever existed. The lumen is slightly narrowed at the site of the former diverticulum. The outline is very smooth." Patient discharged, cured, twenty-four days after operation.

Case IX.—J. C. L., male, aged fifty-nine years. Chief complaints: Difficulty in swallowing food, solid and liquid, regurgitation of liquids and particles of food between meals. He has lost much weight. The first symptoms were noticed five years ago. He consulted a number of physicians and various diagnoses were made. He was unable to work, was practically confined to bed just previous to his admission to the hospital. *X*-ray and esophagoscopic examinations disclosed a well-developed diverticulum springing from the usual site.

*Operation.* Preliminary gastrostomy and the combined Gaub-Jackson operation were performed at the same seance. The sac was exposed and found to be densely adherent. The sac was amputated at the esophagus. The esophageal wall was reinforced.

*Postoperative Treatment.* Patient was fed through the gastrostomy tube. Stitches were removed from the neck on the tenth day. There was a slight discharge from the deep tissues of the neck. This persisted for five days, after which the wound healed rapidly. One month after the operation the gastrostomy tube was removed and gastric fistula was permitted to heal. The neck wound healed entirely eighteen days after the operation. *X*-ray examination on the twenty-second day disclosed no evidence that an esophageal diverticulum had ever existed. Patient was discharged in good condition and has since gained thirty-five pounds in weight.

Case X.—A. A. N., male, aged fifty-six years. Chief complaints: Dysphagia for solid food, slight hoarseness, loss of 10 pounds in weight. Present illness dates back one and a half years, at which time while eating toast he had a severe choking attack, following which he developed fever, difficulty in swallowing and a severe pain in the neck. Since this attack he has been unable to swallow solid food. *X*-ray examination disclosed a small diverticulum, the sac reaching to a little above the upper border of the sternum. The diverticulum is irregular in its lateral borders and presents somewhat to the right of the median line. Owing to the difficulty in swallowing we were unable to get information as to the size of the opening. The esophagus below this point is entirely normal. This case is shown in Fig. 6 as a traction diverticulum. Preliminary gastrostomy and the combined Gaub-Jackson operation performed at the same seance. There were extensive periesophageal adhesions. The pouch was found to be adherent to the under surface of the thyroid gland. The esophagus was drawn into irregular folds around the diverticulum. The sac was dissected from the dense adhesions and the irregularity of the esophagus unfolded, the sac was fixed to the deep cervical fascia so that the fundus presented at a higher level than the opening.

*Postoperative Treatment.* The patient's convalescence was uninterrupted. The gastrostomy tube was removed three weeks after the operation. The

cervical wound healed by first intention. *X*-ray examination, following the operation, by Dr. Manges: "There is a small quantity of barium retained in a little pouch at the level of the first dorsal vertebra. It has a wide opening and does not interfere with swallowing." On the patient's discharge from the hospital he was able to eat regular house diet.

Case XI.—J. G. R., male, aged sixty-nine years. Chief complaints: Lodgment of food in the esophagus, gurgling noise on deglutition, regurgitation of food. Loss of considerable weight. Present trouble dates back four years. *X*-ray examination and esophagoscopic examinations, by Dr. Manges and Dr. Jackson, disclosed a diverticulum at the usual level, slightly larger than the average sac. Preliminary gastrostomy was performed, with the combined Gaub-Jackson operation for diverticulum of the esophagus by Dr. Clerf and Dr. Shallow. Primary amputation of the sac with reinforcement of the esophagus was done in one stage. The wound was closed except for a small drain of cello-silk at the lower angle.

*Postoperative Treatment.* Ten days after the operation the stitches and cello-silk were removed. The wound healed by primary intention except for the small opening left after the drain had been removed. Twenty-one days after the operation the gastrostomy tube was removed and the patient was allowed to eat regular house diet. Twenty-four days after operation, *x*-ray examination disclosed no evidence of a diverticulum. There is a slight narrowing of the esophagus at the site of the operation.

Case XII.—A. J. B., male, aged sixty-five years. Chief complaints: Huskiness of voice, occasional regurgitation of particles of food, gurgling noise on swallowing and loss of weight. *X*-ray and esophagoscopic examinations made by Dr. Manges and Dr. Jackson disclosed a diverticulum of the esophagus a little below the cricoid cartilage. The sac projects a little more to the right than usual.

*Operation.* Combined Gaub-Jackson operation for diverticulum of the esophagus by Dr. Jackson and Dr. Shallow. The sac was removed. The wound in the esophagus was reinforced after suturing. It was a one-stage operation.

*Postoperative Treatment.* The patient was fed through a Rehfuss tube during his convalescence, which lasted twenty-two days. On the tenth day the stitches and cello-silk drain were removed. Twenty-one days after operation *x*-ray examination, by Dr. Manges, showed that there was no evidence that a diverticulum had ever existed. Patient discharged able to eat house diet.

Case XIII.—R. B. H., aged fifty-seven years. Chief complaint: Slight regurgitation of small particles of food after meals, with gurgling noise in neck. Present illness dates back four years. He has not lost any weight. Bronchoscopic examination, by Dr. Jackson, disclosed a small diverticulum springing from the usual site. Operation under combined Gaub-Jackson method. The sac was found to be small and the neck of it was narrow. The neck of the sac was twisted and the fundus was sutured to the deep cervical fascia and the incision closed.

*Postoperative Treatment.* No Rehfuss tube was used because the sac was not amputated. Liquid food was given by mouth on the second day. Solid food was given on the eighth day. Uneventful convalescence.

CONCLUSIONS. 1. The use of the esophagoscope while the surgeon is doing his work (Gaub-Jackson operation) is the operation of choice for the following reason: (*a*) Aspiration pneumonia is practically eliminated. (*b*) The easy access to the sac by the use of the esophagoscope distinctly limits the dissection and hence lessens the probability of mediastinitis. (*c*) By transillumination and protrusion of the sac on the esophagoscope the structure is quickly identified and its fundus found. (*d*) The time of operation is shortened fully one-half.

2. The reef stitches, by slightly narrowing the esophagus, move the point of contact of the bolus of food to a higher level, so that when food is passing over the old site of the diverticulum it does so with a greater velocity than normal and the pulsion pressure is less. This phenomenon is demonstrated by fluoroscope examination following healing.

3. The reef stitches reinforce the weak triangular area over the buried stump. Without such reinforcement a potential factor in recurrence of the diverticulum remains.

4. The one-stage operation offers the best possibility for permanent repair, because in a two-stage operation the repair is made in much inflammatory tissue. The two-stage operation is somewhat safer, but far less apt to effect a permanent cure.

5. Diverticula do not all spring from the same level. This is exemplified by Case III, the double diverticula. Diverticula may exist at birth, be present in youth and persist for years undiagnosed.

6. Fistula following operation is more frequent after the two-stage than the one-stage method.

7. For postoperative feeding the Rehfuss tube is passed through the nose and into the stomach and is retained for many days in order to afford rest to the esophagus and to prevent leakage. This method is superior to feeding by way of a gastrostomy. In Case XIII no gastrostomy was made and the Rehfuss tube was not used.

8. Intratracheal ether insufflation is invaluable in the operation for esophageal diverticulum. We use no other method of anesthesia in these cases at the Jefferson Hospital.

9. There were no fatalities in this series of cases.

10. In our series of 13 cases there was 1 female. This is in accordance with the accepted opinion that diverticula are much more common in males than females.

11. The oldest patient was aged sixty-nine years. The youngest patient to manifest symptoms of diverticula at the age of thirteen years was aged fifty-four years when he came to operation.

12. The average age of patients was between fifty-five and sixty-five years.

NOTE.—Since presenting this paper we have had 2 additional cases, 1 of whom made an uneventful recovery, the other patient died on the third day of a massive collapse of both lungs.

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## DISCUSSION

DR. WILLIS F. MANGES: I am glad to discuss this paper by Dr. Shallow and Dr. Jackson on "The Treatment of Esophageal Diverticula," because I have had the opportunity and privilege of studying the patients that Dr. Shallow and Dr. Jackson have operated. I am strongly impressed with the very fine results that have been obtained in quite a large percentage of the operated cases. In many of them the diverticulum has been completely removed, with no evidence that there ever had been anything wrong with the esophagus except possibly a slight gradual narrowing of the barium-filled esophagus at the level of the operation. In other instances it was absolutely impossible to tell from the fluoroscopic study or from films that there ever had been a lesion of any kind involving the esophagus. In one instance that I have in mind a small portion of the sac remained after operation. This gradually enlarged, so that at the end of a year following the operation the diverticulum was again as large as it had been originally. In another instance a rather large portion of the sac

remained after the first operation, but was completely removed at a second operation, following which there was absolutely no evidence that there had been any lesion in the esophagus. The barium column was perfectly smooth on all sides and of normal diameter throughout. In still another instance there was a double diverticulum: One very large pouch filled up and before it was completely filled a second pouch began to appear on the opposite side. This second pouch, at evidently a little higher level, was found to be of not more than half the size of the larger one. One sac was completely removed at operation, following which there was the *x*-ray evidence of an ordinary esophageal diverticulum and it was not possible to tell that there had been another sac present.

The diagnosis of this condition is usually made before the roentgenologist sees the patient, although we do occasionally find a diverticulum when some other organic lesion is suspected. In one instance that I recall, the patient had had instruments passed to dilate a stricture over a considerable period of time. What he had was an ordinary, fairly large diverticulum.

The roentgenologist may be of help to the surgeon by demonstrating to him (1) the size of the sac, and (2) its location, as to whether it points to the right or to the left and approximately when possible (and it sometimes is) the size of the opening.

There is also some slight variation in the level at which the diverticulum is found—that is, it is most commonly at about the level of the pharyngo-esophageal junction—but I feel confident that it is distinctly lower than this at times. The traction type of diverticulum may be found in any portion of the esophagus. I have seen one that came from the left anterior portion of the esophagus and projected downward, outward and slightly forward into a narrow, conical-shaped sac, with the point of the cone away from the esophagus. They are not uncommon in the lower third of the esophagus, where they may attain a considerable size, but, as a rule, produce no symptoms.

The *x*-ray study is made by means of the fluoroscope, as well as by means of films or plates. A well-lighted fluorescent screen gives probably the most information because one sees all of the mechanics involved in the act of swallowing, whereas a film exposure is a record of an extremely short portion of time. Observations should, of course, be made in both the anteroposterior and oblique or as nearly lateral position as possible, and the best results are always obtained with the patient in the erect posture.

# EFFECT OF VARIOUS AGENTS—ULTRAVIOLET LIGHT, VACCINES, TURPENTINE, NEOARSPHENAMIN AND AUTOBLOOD INJECTIONS—ON THE ENZYMES OF BLOOD AND SKIN*

A PRELIMINARY REPORT

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Within recent years, many physical agents and various nonspecific protein injections have been advocated in the treatment of cutaneous diseases and in other general morbid conditions. The roentgen-rays and ultraviolet light have been employed in many skin diseases and, likewise, in tuberculosis, cancer, leukemia and other diseases. Vaccines, both specific and nonspecific, have been extensively used in many infections. Oil of turpentine has been employed to raise the resisting power of the organism in pyogenic conditions. Autoserum and autoblood injections have been successfully employed in psoriasis and in certain other dermatoses. Many other nonspecific protein injections have been credited with desirable therapeutic effects.

In view of the free employment of these various agencies, we have thought it worth while to endeavor to study the influence of some of them on that relatively little explored field, the enzymes of the body. We have largely limited our investigations to a study of the lipase and protease in the blood and in the skin.

The lipase determinations were numerically greater than the protease for the reason that, to obtain a sufficient quantity of blood for the latter, the laboratory animal had to be sacrificed. It was obviously impossible, with the method employed by us, to make

* Read March 4, 1925.

comparative studies of the skin enzymes before and after treatment, as this could be determined only after the death of the animal.

Effect of Ultraviolet Light. Ten rabbits were, at various times, exposed to ultraviolet light (Alpine lamp). The rabbits weighed about 2 kg. These were usually exposed at a distance of 10 inches (25.4 cm.) in such a manner as to permit irradiation of the greater part of the body. The exposure was usually twenty minutes. Many of the animals were exposed a second, third, fourth and fifth time, at intervals of a few days.

Effect on Lipolytic Ferment (Lipase). In Table I, Rabbit 1 showed a titer of 37 before exposure. Seventeen hours after a twenty-minute exposure, it was 29; four hours after the second exposure, 23; forty-eight hours after the second exposure, 24; four hours after the third exposure, 22; seventy-two hours after the third exposure, 30, and four hours after the fourth exposure, 28. There was, therefore, a reduction from 37 to 28 after four exposures.

Rabbit 2 showed a reduction in lipase titer from 99 to 72, after five exposures.

Rabbit 3, after five exposures, exhibited a fall from 70 to 40.

Rabbit 4, after four exposures, showed a decline from 49 to 20.

Rabbit 9 (Table II) was sensitized before exposure by an intraperitoneal injection of quinine sulphate. After three exposures, there was a slight decline in the lipase titer from 10.8 to 9.

Rabbit 10 was sensitized by the intraperitoneal injection of eosin. After three exposures, there was a decline from 5.4 to 2.2.

Effect of Ultraviolet Light on Proteolytic Ferment (Protease) in Blood. Rabbit 5 (Table I) showed a rise of from 5 to 11, four hours after the first exposure, but a decline to 5 after the second.

Rabbit 6 exhibited a decline in protease from 15 to 4 after two exposures.

Rabbit 7 showed a rise from 6 to 14 after the first exposure, and a decline to 8 after the second exposure.

Rabbit 8 (Table II), sensitized with eosin, showed a rise from 6 to 24, and then a decline to 10.

In a general way, it may be said that ultraviolet light, in the degree that we applied it, appeared to decrease the lipase in the serum of rabbits and to increase the protease. Further, the effects of the exposures seemed temporary, the tendency being for the values to return to their original levels.

TABLE I.—EFFECT OF ULTRAVIOLET LIGHT ON BLOOD-SERUM ENZYMES OF RABBITS (ALPINE LAMP)

| Rabbits. | Treatment. | Blood. | | Skin. | |
|---|---|---|---|---|---|
| | | Proteolytic activity; mg. noncoagulable nitrogen per 100 cc. | Lipolytic activity; cc. tenth-normal sodium hydroxid per 100 cc. | Proteolytic activity; mg. noncoagulable nitrogen per 100 gm., dry. | Lipolytic activity; cc. tenth-normal sodium hydroxid per 100 gm., dry. |
| 1. | Before | .. | 37 | | |
| | 3.5 hours after Alpine lamp, 10 in., 20 min. | .. | 30 | | |
| | 17 hours after first exposure | .. | 29 | | |
| | 4 hours after second exposure | .. | 23 | | |
| | 48 hours after second exposure | .. | 24 | 4200 | 95[1] |
| | 4 hours after third exposure | .. | 22 | | |
| | 72 hours after third exposure | .. | 30 | | |
| | 4 hours after fourth exposure | .. | 28 | | |
| 2. | Before | .. | 99 | | |
| | 4 hours after Alpine lamp, 10 in., 20 min. | .. | 85 | | |
| | 72 hours after first exposure | .. | 88 | | |
| | 4 hours after second exposure | .. | 80 | | |
| | 3 weeks after second exposure | .. | 100 | | |
| | 4 hours after third exposure | .. | 80 | 5500 | 98[1] |
| | 48 hours after third exposure | .. | 80 | | |
| | 4 hours after fourth exposure | .. | 80 | | |
| | 1 week after fourth exposure | .. | 90 | | |
| | 4 hours after fifth exposure | .. | 72 | | |
| 3. | Before | .. | 70 | | |
| | 4 hours after Alpine lamp, 10 in., 20 min. | .. | 62 | | |
| | 3 weeks after first exposure | .. | 65 | | |
| | 4 hours after second exposure | .. | 60 | | |
| | 48 hours after second exposure | .. | 63 | | |
| | 4 hours after third exposure | .. | 63 | 4000 | 70 |
| | 1 week after third exposure | .. | 61 | | |
| | 4 hours after fourth exposure | .. | 55 | | |
| | 24 hours after fourth exposure | .. | 60 | | |
| | 2 hours after fifth exposure (1 hour) | .. | 40 | | |
| 4. | Before | .. | 49 | | |
| | 4 hours after Alpine lamp, 10 in., 20 min. | .. | 38 | | |
| | 48 hours after first exposure | .. | 31 | | |
| | 4 hours after second exposure | .. | 28 | | |
| | 1 week after second exposure | .. | 36 | 3500 | 50 |
| | 4 hours after third exposure | .. | 30 | | |
| | 24 hours after third exposure | .. | 35 | | |
| | 2 hours after fourth exposure (1 hour) | .. | 20 | | |
| 5. | Before | 5 | | | |
| | 4 hours after Alpine lamp, 10 in., 20 min. | 11 | | | |
| | 24 hours after first exposure | 7 | | | |
| | 4 hours after second exposure | 5 | | | |
| 6. | Before | 15 | | | |
| | 1 hour after Alpine lamp, 10 in., 20 min. | 6 | | | |
| | 24 hours after first exposure | 4 | | | |
| | 4 hours after second exposure | 4 | | | |
| 7. | Before | 6 | | | |
| | 3 hours after Alpine lamp, 10 in., 20 min. | 14 | | | |
| | 24 hours after first exposure | 12 | | | |
| | 4 hours after second exposure | 8 | | | |

[1] Skin scaling.

TABLE II.—EFFECT OF ULTRAVIOLET LIGHT ON BLOOD-SERUM ENZYMES OF RABBITS PREVIOUSLY TREATED WITH PHOTOSENSITIZERS

| Rabbits. | Treatment. | Proteolytic activity; mg. nitrogen per 100 cc. | Lipolytic activity; cc. tenth-normal sodium hydroxid per 100 cc. | Remarks.[1] |
|---|---|---|---|---|
| 8. | 30 mg. eosin per kilogram 30 minutes before exposure to Alpine lamp, 10 inches, 20 minutes | 6 | | |
| | 1 hour after exposure | 24 | | |
| | 24 hours after exposure | 18 | | |
| | 4 hours after second exposure | 10 | | |
| 9. | 10 mg. quinin sulphate per kilogram 30 minutes before exposure to Alpine lamp, 10 inches, 20 minutes | .. | 10.8 | |
| | 1 hour after exposure | .. | 8.8 | |
| | 48 hours after exposure | .. | 10.7 | |
| | 1 hour after second exposure | .. | 10.6 | 20 mg. of quinin sulphate per kilogram, ½ hour before exposure. |
| | 48 hours after second exposure | .. | 10.8 | |
| | 2 hours after third exposure | .. | 9.0 | 20 mg. of quinin sulphate per kilogram, ½ hour before exposure. |
| 10. | 10 mg. eosin per kilogram 30 minutes before exposure to Alpine lamp, 10 inches, 20 minutes | .. | 5.4 | |
| | 1 hour after exposure | .. | 4.1 | |
| | 48 hours after exposure | .. | 4.2 | |
| | 1 hour after second exposure | .. | 3.0 | 30 mg. of eosin per kilogram ½ hour before exposure. |
| | 48 hours after second exposure | .. | 3.4 | |
| | 1 hour after third exposure | .. | 2.2 | 30 mg. of eosin per kilogram ½ hour before exposure. |

[1] Both the eosin and quinin sulphate were injected intraperitoneally. In the control animals, neither appeared to modify the enzyme activity.

Effect of Ultraviolet Light on the Blood Enzymes of Human Subjects. Patient 1 (Table IV), suffering from psoriasis, was exposed to the Alpine lamp (chest and back) for sixteen minutes. A marked reaction (sunburn) developed. The lipase declined from 11 to 7 and the protease from 8 to 6.

Patient 2, suffering from psoriasis, received the same exposures. The lipase declined from 11 to 8, and the protease remained unal-

tered. Patient 3, suffering from generalized pruritus, was exposed for twenty minutes. The lipase rose from 10.5 to 12.5, and the protease from 8 to 9.

Owing to the paucity of observations on human subjects, no definite deductions can be drawn. In 2 of the patients out of 3, there was a decline in the lipase.

TABLE III.—EFFECT OF VARIOUS AGENTS (TURPENTINE, VACCINES AND NEOARSPHENAMIN) ON BLOOD-SERUM ENZYMES OF RABBITS

| Rabbits. | Treatment. | Proteolytic activity; mg. noncoagulable nitrogen per 100 cc. | Lipolytic activity; cc. tenth-normal sodium hydroxid per 100 cc. |
|---|---|---|---|
| 12. | Before | . | 20 |
| | 4 hours after intramuscular injection of 5 cc. turpentine-olive-oil emulsion | .. | 26 |
| 13. | Before | 3 | |
| | 4 hours after intramuscular injection of 5 cc. turpentine-olive-oil emulsion | 5 | |
| 14. | Before | .. | |
| | 2 hours after subcutaneous injection of staphylococcic vaccine | .. | 35 |
| 15. | Before | .. | 30 |
| | 4 hours after subcutaneous injection of staphylococcic vaccine | .. | 35 |
| 16. | Before | 5 | 28 |
| | 4 hours after subcutaneous injection of staphylococcic vaccine | 7 | |
| 17. | Before | .. | 40 |
| | 2 hours after intravenous injection of neoarsphenamin, 50 mg. per kilogram | .. | 37 |
| 18. | Before | 4 | |
| | 4 hours after intravenous injection of neoarsphenamin, 50 mg. per kilogram | 3 | |
| | 24 hours after injection | 4 | |
| 19. | Before | .. | 72 |
| | 5 hours after intravenous injection of neoarsphenamin, 50 mg. per kilogram | .. | 51 |
| | 24 hours after injection | .. | 59 |
| | 72 hours after injection | .. | 69 |

EFFECT OF INJECTIONS OF TURPENTINE, IN RABBITS AND HUMAN BEINGS, ON THE BLOOD ENZYMES. The intramuscular injection of turpentine in 5 cc. of olive oil into a rabbit was followed, in four hours, by a rise of lipolytic activity from 20 to 26. In another rabbit, the proteolytic activity rose from 3 to 5.

In a patient suffering from eczema, the intramuscular injection of 5 minims (0.3 cc.) of rectified turpentine in 5 cc. of olive oil was followed, in three hours, by a rise of lipolytic activity from 9 to 10, and in proteolytic activity from 8 to 10.

In a case of pemphigus, the same treatment was followed, in three hours, by a rise in lipolytic activity from 10 to 14.5, and in proteolytic activity from 6 to 8.5.

In a case of lupus erythematosus, the injection of turpentine was followed, in three hours, by a rise in lipolytic activity from 9 to 14, and in proteolytic activity from 5 to 7.

It would appear from the foregoing studies that the intramuscular injection of turpentine tend to increase the lipolytic and proteolytic power of the blood serum in both rabbits and human beings.

Influence of Vaccines on Blood Enzymes in Rabbits. Rabbit 14 received an injection of staphylococcic vaccine subcutaneously. Two hours later, the lipolytic activity of the blood had risen from 28 to 35.

Rabbit 15, treated in the same manner, showed a rise from 30 to 35, at the end of four hours.

Rabbit 16, treated with staphylococcic vaccine, showed, at the end of four hours, a rise in proteolytic activity from 5 to 7. As far as any deduction from these few experiments with vaccines is permitted, it can be stated that a tendency to rise in both lipolytic and proteolytic activity is suggested.

Effect of Injections of Neoarsphenamin on the Blood Enzymes of Rabbits. Three rabbits were injected intravenously with neoarsphenamin, 50 mg. per kilogram of body weight. This, of course, is a very large dose equivalent to 3 grams for a man weighing 60 kg.

In Rabbit 17, the lipolytic activity, after two hours, was reduced from 40 to 37.

Rabbit 18 received 50 mg. per kilogram of neoarsphenamin. At the end of four hours, the proteolytic power of the serum was reduced from 4 to 3. Twenty hours later, it rose again to 4.

In Rabbit 19, the lipolytic activity was reduced from 72 to 51 at the end of five hours, rising to 59 after twenty-four hours and 69 after seventy-two hours. It would appear that, in rabbits, large doses of neoarsphenamin tend to depress the lipolytic and proteolytic activity of the blood serum.

TABLE IV.—EFFECT OF NONSPECIFIC AGENTS ON BLOOD-SERUM ENZYMES OF HUMAN BEINGS

| Case. | Diagnosis. | Treatment. | Proteolytic activity; mg. noncoagulable nitrogen per 100 cc. | Lipolytic activity; cc. tenth-normal sodium hydroxid per 100 cc. |
|---|---|---|---|---|
| 1 | Psoriasis | Before | 5 | 8 |
| | | 4 hours after intramuscular injection of 20 cc. autoserum[1] | 9 | 19 |
| | | 24 hours after injection | 7 | 17 |
| | | 72 hours after injection | 6 | 15 |
| | | 4 hours after second injection | .. | 21 |
| 2 | Pruritus | Before | . | 8 |
| | | 4 hours after intramuscular injection of 20 cc. autoserum[2] | .. | 14 |
| 3 | Pruritus | Before | 7 | 9 |
| | | 2.5 hours after intramuscular injection of 20 cc. autoserum | 12 | 11 |
| 4 | Psoriasis | Before | .. | 7 |
| | | 3 hours after intramuscular injection of 20 cc. autoserum | .. | 12 |
| 5 | Psorias s | Before[3] | 10 | 7 |
| | | 4.5 hours after intramuscular injection of 20 cc. autoserum | 17 | 8 |
| | | 10 days after injection | 7 | 8 |
| | | 6 hours after second injection serum | 5 | 8 |
| 6 | Eczema | Before | 8 | 9 |
| | | 3 hours after intramuscular injection of 5 m. turpentine in olive oil | 10 | 10 |
| 7 | Pemphigus | Before | 6 | 10 |
| | | 3 hours after intramuscular injection of 5 m. turpentine in olive oil | 8.5 | 14.5 |
| 8 | Lupus erythematosis | Before | 5 | 9 |
| | | 3 hours after intravenous injection of 5 m. turpentine in olive oil | 7 | 14 |
| 9 | Psoriasis | Before | 8 | 11 |
| | | 2 hours after Alpine lamp, 16 minutes' exposure back and front[4] | 8 | 8 |
| 10 | Psoriasis | Before | 8 | 11 |
| | | 2 hours after Alpine lamp, 15 minutes' exposure back and front[4] | 8 | 8 |
| 11 | Acne | Before | 10 | 8 |
| | | 2 hours after Alpine lamp exposure for 10 minutes[5] | 11 | 8 |
| 12 | Pruritus | Before | 8 | 10.5 |
| | | 2 hours after Alpine lamp exposure for 20 minutes[6] | 9 | 12.5 |
| 13 | Psoriasis | Before | 12 | 6.5 |
| | | 3 hours after intravenous injection of 1.5 cc. distilled water | 10 | 6.5 |
| 14 | Normal | Before | 15 | 11 |
| | | 2 hours after intravenous injection of 1.5 cc. distilled water | 8 | 6 |
| | | 6 days after injection | 12 | 8 |
| | | 2.5 hours after second injection[2] | 8 | 6 |

[1] Mild reaction.
[2] Reaction.
[3] Temperature, 100° F.; chills.
[4] Marked cutaneous reaction.
[5] Treatment applied to face.
[6] Cutaneous reaction.

THE EFFECT OF INTRAMUSCULAR AUTOBLOOD INJECTIONS IN HUMAN BEINGS ON THE SERUM ENZYMES. A patient with psoriasis had 20 cc. of blood withdrawn from a vein and immediately injected into the gluteal muscles. Before the injection, the lipolytic activity of the blood serum was 8. Four hours later, it was 19; twenty-four hours after the injection, it was 17, declining to 15 after seventy-two hours. Four hours after a second injection, at the end of seventy-two hours, it rose to 21.

The proteolytic activity rose from 5 to 9 after four hours, declining to 7 at the end of twenty-four hours, and to 6 at the end of seventy-two hours.

Patient 2, with generalized pruritus, treated with autoblood in the same manner as the preceding case, showed a rise in lipolytic activity at the end of four hours, from 8 to 14.

Patient 3, suffering from generalized pruritus, received an autoblood injection and, at the end of two and a half hours, exhibited a rise in lipolytic activity of his blood serum from 9 to 11, and in proteolytic activity from 7 to 12.

Patient 4 (psoriasis), treated with autoblood injection, showed, at the end of three hours, a rise of lipolytic activity from 7 to 12.

Patient 5 (psoriasis) showed a rise in lipolytic activity from 7 to 8. The proteolytic activity rose after four and a half hours from 10 to 17; ten days later, it was 7. Six hours after a second (intravenous) injection of 13 cc. of autoserum, it was 5.

EFFECT OF ULTRAVIOLET LIGHT ON THE LIPOLYTIC AND PROTEOLYTIC ENZYMES OF THE SKIN IN RABBITS. As the skin of treated rabbits could only be tested, by the method employed by us, after death of the animal, an effort was made to determine the average normal enzyme activities in untreated control animals. The skin of 4 untreated rabbits showed a lipolytic activity, varying from 80 to 100 cc. of tenth-normal sodium hydroxid per hundred grams of dry skin, and a proteolytic activity varying from 6000 to 8000 mg. per hundred grams of dry skin.

Rabbit 2, after five exposures to ultraviolet light, showed a titer of 5500 for proteolytic activity, and 98 for lipolytic activity.

Rabbit 3, after four exposures to ultraviolet light, showed a titer of 4000 for proteolytic activity, and 70 for lipolytic activity.

Rabbit 4, after four exposures, showed a titer of 3500 for proteolytic activity and 50 for lipolytic activity.

The foregoing studies would seem to warrant the conclusion that

exposure to ultraviolet light depresses the proteolytic and the lipolytic activity of the skin of rabbits, the former being influenced more than the latter.

Since the normal lipolytic values of the blood in our rabbits appear to be subject to wide individual variations, the same may be true of the rabbit skin. The figures submitted, therefore, in the determinations of enzyme activity in the four normal rabbit skins are given with reservation.

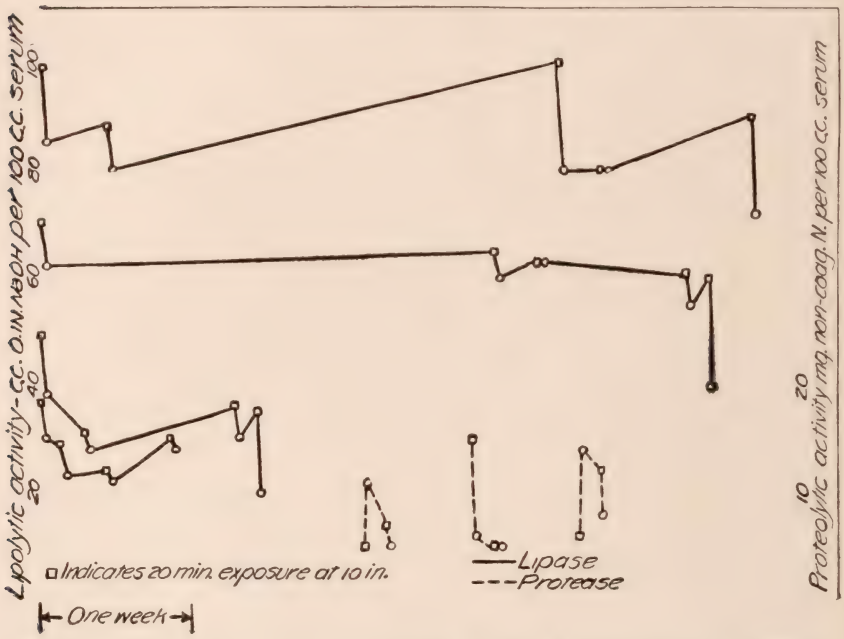


CHART 1.—Course of lipolytic and proteolytic activity of the blood serum of rabbits under influence of ultraviolet light.

EFFECT OF INTRAVENOUS INJECTION OF DISTILLED WATER. A patient suffering from muscular pains was given 1.5 cc. of distilled water intravenously. Before the injection, the lipolytic activity was 11; two hours later, it declined to 6. Six days later, it was 8. Two and a half hours after a second injection, it declined again to 6.

The proteolytic activity, before the injection, was 15. After two hours, it declined to 8. At the end of six days, it was 12. Two and a half hours after a second injection, it was reduced to 8.

Another patient suffering from psoriasis received an intravenous injection of 1.5 cc. of distilled water. At the end of three hours, the lipolytic titer declined from 12 to 10, and the proteolytic titer remained the same, at 6.5.

METHODS. The following modifications of the methods of Jobling, Petersen and Eggstein[1] for serum protease and lipase were used:

*Serum Protease.* To 1 cc. of clear, hemoglobin-free serum in an 18-mm. diameter tube, graduated at 10 cc., were added 2 cc. of chloroform. The tube was shaken sharply until a milky emulsion was formed. A control tube containing 1 cc. of serum was heated on the water-bath for thirty minutes at 60° C., after which 0.5 cc. of toluene was added. Both tubes were stoppered with cotton and incubated for forty-eight hours at 37° C. From time to time, the chloroform tube was shaken to maintain the emulsion. Two cubic centimeters of water were then added to each tube, and 1 cc. of a 20 per cent solution of sodium chlorid in 10 per cent acetic acid. Both tubes were then warmed to remove the chloroform and toluene and placed in boiling water for ten minutes. The tubes were then cooled, diluted to 10 cc., filtered, and the nitrogen determined on 5 cc. of the titrate by the usual micro method. The difference in the nitrogen values, calculated to 100 cc. of serum, is a measure of the proteolytic activity of the serum.

*Serum Lipase.* One cubic centimeter of blood serum, 1 cc. of neutral (phenolphthalein) ethyl butyrate, 1 cc. of toluene and 7 cc. of 0.85 per cent salt solution were placed in a 100 cc. Erlenmeyer flask. To another flask were added 1 cc. of ethyl butyrate, 1 cc. of toluene and 8 cc. of 0.85 per cent salt solution. To a third flask were added 1 cc. of blood serum, 1 cc. of toluene and 8 cc. of 0.85 per cent salt solution. Each flask was shaken 100 times, stoppered with cotton and incubated at 37° C. for four hours. The flasks were then placed in ice-water, 15 cc. of neutral alcohol and 4 drops of a 1 per cent alcoholic solution of phenolphthalein added to each and then titrated rapidly with tenth-normal sodium hydroxid. The titer, corrected for the blanks, when calculated to tenth-normal per hundred cubic centimeters, was taken as a measure of the lipolytic or esterase activity.

The skin enzymes were determined according to the methods of

[1] Jour. Exper. Med., 1915, xxii, 129.

Sexsmith and Petersen[2] except that a 1 per cent skin suspension was used.

The proteolytic activity was determined by starting with an initial pH of 5.5. For the autolysis, however, the initial reaction of the suspension was not altered.

A search of the literature reveals very sparse data bearing directly on the studies here reported.

Wells[3] says: "In view of the fact that enzymes and antibodies in solution are quite readily weakened or destroyed by the action of light, it is possible that intracellular enzymes may be similarly destroyed by light, with resulting cell death."

Bering[4] found that chemically active light rays have a direct action on oxidizing enzymes.

Burge, Fischer and Neill[5] state that hormones, proenzymes and enzymes are destroyed by exposure to ultraviolet radiation. The rate of destruction is proportional to the amount of energy applied. (Experiments were performed *in vitro,* the enzyme solutions being subjected to long exposures, from one to three hours, and then tried out for activity on definite substrates.)

Jobling and Petersen[6] conclude that the serum ferments are practically unaltered by a primary injection of a foreign protein. Acute shock produces an instantaneous increase in protease, followed later by an increase in serum lipase. They state that the shock is produced by the protease splitting various proteins down to the toxic peptone stage.

Jobling, Petersen and Eggstein[7] found that the intravenous injection of killed organisms is followed by the mobilization of nonspecific protease and lipase; the rapidity and extent of this reaction depend on the toxicity of the organism and on its resistance to proteolysis. The temperature and leukocyte curve bear no relation to the ferment changes.

Pincussen and Anagnostin[8] studied the effect of roentgen-rays and nitra-lamp radiation on the serum lipase. The results, in general, showed that radiation of either the serum or the animal from which the serum was taken reduced the lipase activity. On

[2] Jour. Exper. Med., 1918, xxvii, 273.
[3] Chemical Pathology, Ed. 3, Philadelphia, W. B. Saunders Company, 1918, p. 374.
[4] München med. Wchnschr., 1912, lix, 2975.
[5] Am. Jour. Physiol., 1916, xl, 425.
[6] Jour. Exper. Med., 1915, xxii, 401.
[7] Ibid., 603.
[8] Biochem. Ztschr., 1922, cxxviii, 268.

the other hand, diathermy, as well as galvanism, when applied to the living animal, led to a significant increase.

It has been found that ferments lose their power under strong exposure to light.[9] Ferments may be destroyed by exposure to the visible as well as to the ultraviolet end of the spectrum. Green[10] found that amylase is destroyed by short-wave-length rays. On the other hand, the visible rays activate this enzyme through influence on the zymogen.

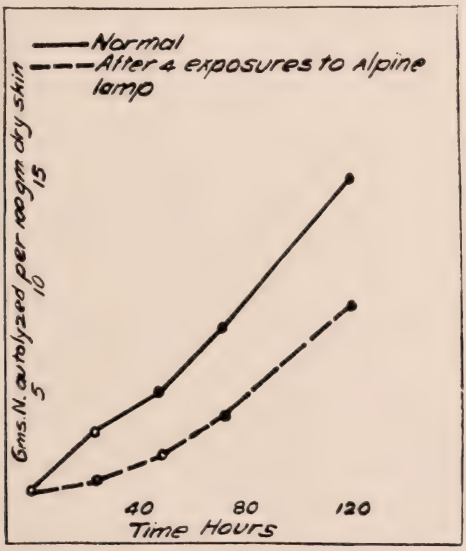


CHART 2.—Comparative autolysis of normal rabbit skin and that of rabbit exposed to ultraviolet light.

Chymosin, katalase and peroxidase, which are but slightly injured by exposure to the visible rays, are readily and permanently made inert by exposure to the short-wave rays. The action of long-wave rays on enzymes was first described by Downes and Blunt, the discoverers of the bactericidal action of light.

Bering and Meyer[11] demonstrated that peroxidase, exposed to light, acquired an increased activity. This was more particularly true of the short-wave lengths.

[9] Hausmann: Grundzüge der Licht-biologie und Pathologie, Berlin, Urban and Schwarzenburg, 1923.

[10] Quoted by Euler: Chemie der Enzyme, München-Wiesbaden, 1920, p. 197.

[11] Strahlen-therapie, 1912, i, 411.

It will be seen from the foregoing references that all these experiments were carried out *in vitro*.

That intracellular ferments may be influenced by light *intra vitam* was shown by the careful researches of Ostwald[12] on the peroxidase and katalase content of different heliotropic animals. The katalase content of living "räupchen" of porthesia chrysorrhea is strikingly lessened by exposure to light. The physiologic production of katalase is apparently favored by green light, but restricted by violet light. The production of peroxidase is stimulated to the same extent that katalase is destroyed.

Pincussen[13] believes that all cells possess their own ferments, which may be thrown into the blood when the cells break up. He states that exposure to light stimulates this.

Conclusions. 1. Ultraviolet light, in the strengths used by us from an Alpine lamp, appears to decrease the lipolytic activity of the blood serum both in rabbits and in human beings. On the other hand, the proteolytic activity of the blood serum appears to be increased.

2. The intramuscular injection of therapeutic doses of turpentine in olive oil tends to increase the lipolytic and the proteolytic power of the blood serum both in rabbits and in human beings.

3. Limited observations on the effect of subcutaneous injections of staphylococcic vaccines suggest that they tend to increase both the lipolytic and proteolytic activity of the blood serum.

4. The intramuscular injection of freshly drawn autoblood appears to stimulate an increase in the lipolytic and proteolytic activity of the blood serum.

5. The injection of large doses of neoarsphenamin in rabbits (equivalent to 3 gm. for a man weighing 60 kg.) tends to depress the lipolytic and proteolytic activity of the blood.

6. Observations on 2 cases suggest that the intravenous injection of small quantities (1.5 cc.) of distilled water tends to decrease the lipolytic activity of the blood and perhaps the proteolytic power.

7. The exposure of rabbits to ultraviolet light from an Alpine lamp decreases the lipolytic and the proteolytic activity in the skin of an animal.

8. In summarizing, it may be said that injections of vaccines, turpentine and autoblood appear to increase the lipolytic and proteo-

[12] Biochem. Ztschr., 1908, x, 1.
[13] Quoted by Hausmann (footnote 9, p. 77).

lytic power in the blood, while huge doses of neoarsphenamin and small doses of distilled water tend to decrease them. Ultraviolet light depresses the lipolytic, and stimulates the proteolytic activity.

## DISCUSSION

Dr. John A. Kolmer: I know of few subjects more complicated and difficult to discuss, in relation to infection and immunity, than the relation which the enzymes bear to disease. During the past few years considerable confusion has resulted by the use of the term "ferments" by Abderhalden, so that antibodies and "ferments" have been rather loosely applied to phenomena of different kinds. But in the paper presented by Dr. Schamberg and Mr. Brown the term has been correctly employed to designate the proteolytic and lipolytic enzymes or ferments of the blood and skin.

It is pertinent to inquire what relation, if any, these two groups of enzymes bear to resistance and immunity. In the first place, three or four different kinds of proteolytic enzymes have been described in the blood, some of which are derived from leukocytes, and since some of the agents reported upon this evening are known to produce leukocytosis, probably by colloidal shock stimulation of the bone-marrow, it is reasonable to surmise that a part of the increase of blood protease is due to an increase of these leukocytic enzymes. The lipases of the plasma may also undergo an increase, but our knowledge of their source and the mechanism involved is quite incomplete.

But in the present discussion we may properly inquire as to what relation, if any, the proteases and lipases of the blood bear to infection and treatment.

It is possible and probable that these ferments may actually destroy some organisms or at least reduce the resistance of bacteria and render them more vulnerable to other destructive agencies. It is believed by some, for example, that lipases may aid the penetration of tubercle bacilli by chemotherapeutic agents. But while the influence of these enzymes upon living organisms may be doubtful, there can be no doubt of their ability to digest dead organisms, providing sufficient amount of antiferment has been removed.

Some of the agents reported upon this evening by the essayists are commonly employed for purposes of nonspecific protein therapy. The mechanism involved is not definitely known, but it is highly probable that these agents are sometimes beneficial in the treatment of infectious diseases through the production of leukocytosis, an increase of the enzymes of the blood and possibly by an increase of capillary permeability permitting a freer access of both enzymes and antibodies to localized foci of infection.

It may be also advisable to briefly refer to the skin in relation to immunity. Several investigators have placed considerable emphasis on this

organ as not only vitally concerned in resistance to infection through the mechanical barrier of epithelium, but likewise through the agency of enzymes to be found in the skin. Some are of the opinion that organisms brought to the skin are destroyed by these agencies. It is frequently stated, therefore, that in the exanthematous diseases a well-marked exanthem is an indication of increased destruction of organisms, which may spare the internal organs and favorably influences prognosis.

These and additional factors lend great interest to the presentation by Dr. Schamberg and Mr. Brown, and at least serve to emphasize the importance that the skin bears to certain processes in resistance and immunity to disease and how various forms of light and protein therapy may exert favorable therapeutic effects.

# INTRAVENOUS INJECTION OF MERCUROCHROME-220 FOR BLOOD-STREAM INFECTIONS IN THE PUERPERIUM*

By BARTON COOKE HIRST, M.D.

There has been a lamentable lack of progress in the treatment of puerperal blood-stream infections. In answer to a questionnaire sent to the principal maternity clinics of the country no constructive suggestions were received except from Polak's Clinic in Brooklyn, where repeated small blood transfusions were being employed. The spirit pervading most of the replies was reflected in one that stated, "We put these cases on the roof and forget them." There is little additional knowledge to be gained from reading the transactions of the Congress on Puerperal Fever held in Strasburg in August, 1923.

The work, therefore, of Dr. E. B. Piper in the Pepper Laboratory and the Maternity Department of the University of Pennsylvania, begun in February, 1920, and continued ever since, deserves careful attention.[2]

Many attempts have been made to disinfect the blood in blood-stream infections and many agents have been employed; colloidal silver, arsenobenzol, formaldehyde, bichloride of mercury, phenol preparations, ammoniated sulphate of copper, etc., but the minimum toxic dose was not determined, laboratory investigations have been neglected, and the clinical results have been unconvincing.

On November 15, 1919, Dr. Hugh Young described a new antiseptic, mercurochrome-220, the result of some two years' work to develop an antiseptic suitable for local application in the genito-urinary tract.

Dr. Piper's attention being called to this substance, he began in February, 1920, a laboratory investigation as to its efficacy in

* Read March 4, 1925.

[2] Reported to the Am. Gynec. Soc., by invitation, May 1 to 3, 1922.

sterilizing an infected blood stream, a use to which it had not hitherto been put. The results of these experiments were reported, as already stated, May 1 to 3, 1922.

After establishing the minimum toxic dose, the dilution in the blood necessary to destroy streptococci *in vitro* and *in vivo*, the clinical application of this information was begun in April, 1920. At first only the most desperately ill women, apparently moribund, were selected for this treatment; but as confidence in its safety and efficacy increased, it was made the routine treatment of the serious blood-stream infections in the Maternity Department of the University Hospital.

The following cases, treated by Dr. Piper, and under my observation, are appended:

Case I.—Mrs. S., admitted April 30, 1920. The patient was delivered two weeks previous to admission and had been well until three days before her admission to the University Hospital, when she developed a high fever, rapid pulse and rapid respiration, and chills. On admission her temperature was 105° F., pulse-rate 162, and respiratory rate 52. The patient was practically moribund. A blood culture was taken immediately after admission, and was later reported loaded with colonies of hemolytic streptococci. The patient was given one injection of 30 cc. of a 1 per cent mercurochrome solution intravenously. She had no reaction to the drug and died the next morning.

Case II.—Mrs. A. V., aged nineteen years, Italian; Para-0. Admitted in active labor June 29, 1920. The patient was very apprehensive and had an ashen-gray color in her face. Low forceps were applied, and the patient delivered of a stillborn baby, which appeared to have been dead about twenty-four hours. Because of her high temperature, rapid pulse and rapid respirations, and other signs of infection, a blood culture was taken and later reported as showing colonies of nonhemolytic streptococci. On July 6, 1920, the patient was given an intravenous injection of a 1 per cent mercurochrome solution in a dose of 5 mg. per kilo of body weight. The patient had no reaction to the drug and no ill or beneficial effects were noted. The patient died a few hours later. It should be noted that no July 5, one day before the mercurochrome was administered, this patient had received 100 cc. of antistreptococcic serum without any beneficial effects.

Case III.—Mrs. H. B., aged thirty-eight years, married nineteen years; Para-IV. Last child four and a half years ago. One miscarriage October 16, 1920. The menstrual history was normal. On admission the patient was suffering with phlegmasia alba dolens. A blood culture taken December 3, 1920, showed the presence of hemolytic streptococci. The patient was given 30 cc. of a 1 per cent solution of mercurochrome intravenously.

She had a sharp chill and a rise of body temperature to 102° F. Following the administration of the drug the pulse-rate rose to 132 and the respiration to 30 per minute. On December 6, 1920, the patient was given 8 cc. of a 1 per cent solution of mercurochrome intravenously. Two days later she was given a third dose of 4 cc. of a 1 per cent solution of the drug. On December 11, 1920, she was given 32 cc. of a 1 per cent solution of mercurochrome intravenously. There was only a slight reaction following it. A blood culture taken December 14, 1920, was sterile. On December 17, the patient received 35 cc. of a 1 per cent mercurochrome solution intravenously. December 20 she was given 32 cc. of a 1 per cent mercurochrome solution intravenously. Following the administration of the drug she had a chill which lasted for twenty minutes, a temperature of 102° F., pulse 132, and respiration of 30. The blood culture was still sterile. The patient died December 24, 1920. Although a cure was not effected, it should be noted that the blood stream was permanently disinfected by the use of mercurochrome intravenously, the first time such a result was obtained from the use of this drug.

Case IV.—Mrs. B., admitted December 20, 1920. Five days after delivery the patient developed a severe chill and stabbing pains in the abdomen. She vomited frequently. When admitted to my service the patient was in a stuporous condition and had generalized peritonitis. Dilatation and evacuation of the uterus was done and laparotomy with drainage performed. The patient was given an intravenous injection of 30 cc. of a 1 per cent mercurochrome solution. She died December 22, 1920.

The use of mercurochrome intravenously in the treatment of puerperal sepsis and septicemia was then discontinued for a period of one year, during which time Dr. Piper made further laboratory studies and investigations. Although the first 4 patients treated by this method all died, still there was some indication that the method was of real value. In 1 patient the blood stream had been effectively and permanently disinfected. This case was of further value in first demonstrating what subsequently proved to be a fact, namely, that beneficial effects are obtained from the intravenous use of mercurochrome only in those cases in which there is a definite reaction following the administration of the drug. It should be remembered also that these patients were extremely sick when admitted to the hospital. The first patient was moribund and lived only a few hours after her admission. The second patient lived seven days. The fourth patient was in a stuporous condition and had generalized peritonitis when admitted. She died two days later. Such cases could scarcely be called a fair test of the efficacy of any method of treatment, and no drug could reasonably be expected to effect a cure under such conditions. In fact, the drug was administered to these patients more for the purpose of observing its action and the patient's reaction to it than in the hope of effecting a cure.

Case V.—Mrs. S., admitted January 4, 1922. Aged twenty-two years, Para-V. Last child born prematurely at eighth month of gestation Decem-

ber 28, 1921. Three days after her delivery the patient developed a severe chill lasting one-half hour. She had a high fever and on her admission to the hospital was in delirium.

A blood culture, taken immediately after her admission, showed hemolytic streptococci. January 8, 1922, the patient received 30 cc. of a 1 per cent solution of mercurochrome intravenously. She had only a slight reaction, but the drug was excreted, as was indicated by normal urine the following day. A blood culture taken two days after the administration of the drug was still positive for hemolytic streptococci, so a second injection of 30 cc. of a 1 per cent mercurochrome solution was given intravenously. Following this injection the patient's temperature rose to 103° F., the pulse was 128, and the respirations 32. This was a fairly good reaction. Two days later (January 12, 1922) the patient received a third intravenous injection of 35 cc. of a 1 per cent solution of mercurochrome. There was no reaction to this dose, but the urine was normal the following day, showing that the kidneys had not been damaged by the drug. January 25, 1922, the drug was again administered in a dose of 50 cc. of a 1 per cent solution. There was a good reaction to this dose, but in spite of this a blood culture taken three days later still showed hemolytic streptococci. Apparently we were not securing the desired results with mercurochrome in this case, so its use was stopped, and on February 4, 1922, the patient was given 100 cc. of polyvalent antistreptococcic serum intravenously. But little reaction was noted following the use of the serum. The patient's condition remained about the same until February 27, 1922, when she developed a suppurative thrombophlebitis in her left leg. This was opened and drained. The patient then began to improve, and a blood culture taken April 13, 1922, was sterile. The patient was discharged in good condition May 13, 1922.

There are several points of interest in this case. As may be seen from the above report the blood stream of this patient was not sterilized by the intravenous use of mercurochrome. Although no explanation of the failure of the drug in this case is required, since we have never claimed it to be effective in all cases, still it seems justifiable to offer the following reason as the probable cause of failure. The focus of infection which eventually manifested itself as a suppurative thrombophlebitis of the left leg was constantly throwing bacteria into the blood stream in large numbers, so that in spite of any action the drug may have exerted, the blood was still infected. Subsequent cases have demonstrated that the blood stream cannot be permanently sterilized so long as an undrained focus of infection exists in the patient. This case is of further interest because of the frequency with which the drug was used. Three doses or a total of 95 cc. of the drug were given within five days, and a total of 145 cc. of a 1 per cent solution of the drug were given within sixteen days, without toxic effects on the patient. Although we have been more cautious in the use of the drug in our recent cases, we have found that the drug may be safely repeated when the urine is clear and free of albumin and casts and the diarrhea is checked. It is, however, quite dangerous to repeat the drug when there is any manifestation of nephritis. Just what part the use of antistreptococcic serum played

in this case is uncertain, but from a study of the clinical course of the case it appears to have had but little, if any, effect.

Case VI.—Mrs. E. D., admitted May 12, 1922. Aged twenty-two years, married six years; Para-II. Last child born in 1920. One miscarriage five years ago. The menstrual history is normal. The last menstrual period began January 9, 1922. April 28, 1922, the patient fell off a step-ladder. That night she began to have cramp-like pains in the abdomen, which continued until the following night, when she miscarried. She felt well until May 4, 1922, when she developed chills and fever and profuse sweats. She also complained of pain in her left groin and back, and had been bleeding off and on ever since her miscarriage. A blood culture taken on admission showed hemolytic streptococci. May 17, 1922, the patient was given 24 cc. of a 1 per cent mercurochrome solution intravenously. There was no chill or definite reaction following the injection, but diarrhea developed, and there was a temporary rise of temperature followed by a marked fall. A blood culture taken May 25, 1922, was sterile. The patient was discharged as cured May 28, 1922.

Case VII.—Mrs. T. B., admitted June 23, 1922. Aged twenty-five years; married twenty-six months; Para-II. Last child born June 13, 1922. The patient had been in active labor for some hours with no progress. High forceps were applied and delivery attempted without success. The patient was then delivered of a stillborn child by version. Two days later she developed soreness in the lower abdomen and high fever. The day before her admission to the hospital she became delirious. On admission her temperature was 103.6° F., pulse 160, respirations 40. The patient was very definitely septic, so, without waiting for a report on a blood culture, she was given 25 cc. of a 1 per cent mercurochrome solution intravenously. There was no definite reaction, but a slight drop in temperature followed the use of the drug. The next day the patient was given 15 cc. of a 1 per cent solution of the drug. There was no noticeable effect on the patient, and death occurred June 25, 1922.

Case VIII.—Mrs. A. R., admitted April 6, 1922. Five days after delivery the patient had a severe chill and developed high fever. A blood culture taken April 11, 1922, showed hemolytic streptococci. The patient was given 25 cc. of a 1 per cent mercurochrome solution intravenously. She had a very good reaction to the drug, her temperature rising to 104° F., pulse 136, and respiration 32. April 27, 1922, the patient received a second dose of 28 cc. of a 1 per cent mercurochrome solution intravenously. Again she had a very good reaction. Her blood culture taken two days later showed no growth. The patient was discharged as cured May 16, 1922.

Case IX.—Mrs. T. Y., admitted September 20, 1922. Aged thirty-two years; Para-V. Last child born three weeks before admission. Three miscarriages, last six years ago. Menstrual history normal. Three weeks previously the patient was delivered of a normal child without

difficulty. Two days later she developed severe pain in both iliac fosæ. The pain lasted one week and then subsided. Nine days later the pain returned with more severity. She suffered considerably and had a high fever. On admission to the hospital her leukocyte count was 14,500. A blood culture taken September 21, 1922, showed nonhemolytic streptococci.

September 25, 1922, the patient received 27 cc. of a 1 per cent mercurochrome solution intravenously. She had a very marked reaction of the usual type. The urine showed that the drug had been well borne by the kidneys, so the next day she was given 15 cc. of a 1 per cent mercurochrome solution intravenously. This dose was followed only by a slight reaction, but the patient seemed clinically much improved. A blood culture taken October 5, 1922, was sterile. About this time an abscess developed in Douglas' cul-de-sac; this was opened and drained October 10, 1922. A culture of the pus from this abscess showed Staphylococcus albus. The patient made an uneventful convalescence and was discharged in good condition November 22, 1922.

Case X.—Mrs. N. B., admitted November 27, 1922. Aged thirty-two years; Para-I. Last child thirteen years ago by difficult instrumental delivery. No miscarriages. Menstraul history normal. Last period June 3, 1922. The patient was about six and a half months pregnant. While doing her housework she attempted to lift a heavy box. Suddenly she began to bleed profusely, and was brought to the hospital after losing considerable blood. The diagnosis of placenta previa was made, and the vagina was firmly packed with gauze. Each time the gauze was removed the bleeding recurred, so finally on December 7, 1922, labor was induced by inserting a bag in the cervix. That night the patient was delivered of a stillborn child by podalic version. Following this she developed high fever, chills, and other signs of septicemia. A blood culture taken December 9, 1922, showed hemolytic streptococci. December 13, 1922, the patient was given 40 cc. of a 1 per cent mercurochrome solution intravenously. She had a fair reaction. Her condition, however, became steadily worse. December 15, 1922, she was given a second dose of 30 cc. of a 1 per cent mercurochrome intravenously. She had no reaction to this dose. Her condition became steadily worse, and she died December 17, 1922.

Case XI.—Mrs. S. R., admitted January 2, 1923. Aged forty years; married twenty-three years; Para-VIII. Last child born two weeks ago. Four miscarriages; last miscarriage five years ago. The patient was delivered at home December 22, 1922. Four days after delivery her lochia stopped and she began to have pain in her lower abdomen. December 29, 1922, she developed chills and fever which continued until the time of her admission to the hospital. The patient had severe headaches and pain in her right thigh, which had been swollen for four days. Blood cultures taken January 4 and January 5, 1923, showed no growth. The urine on admission showed a light cloud of albumin, many hyaline casts, and was loaded with white blood cells. A diagnosis of pyelitis was made. January 6, 1923, the patient received 40 cc. of a 1 per cent mercurochrome

solution intravenously. She had a good reaction to the drug and seemed clinically benefited by it. January 16, 1923, a second dose of 40 cc. of a 1 per cent mercurochrome solution was given intravenously with 100 cc. of normal salt solution. A good reaction followed the use of the drug and the urine cleared up. The patient was discharged as cured March 11, 1923.

Case XII.—Mrs. C. R., admitted April 11, 1923. Aged thirty-nine years; married twenty years; Para-XI. Last child born twelve days ago. Three miscarriages; last miscarriage four years ago. All labors easy and natural. The patient has had a profuse yellowish leucorrhea for many years.

Three days after the birth of her last child the patient developed sharp, shooting pains in her right leg. The pains increased in intensity until April 4, 1923, when an ulcer appeared on the inner surface of the leg. This drained quite freely. About this time she developed high fever and was generally hard hit. The pains in her leg gradually disappeared, but the ulcer continued to drain. On admission her temperature was 103° F., pulse 112, and respiration 28. A blood culture taken immediately after her admission showed an abundant growth of hemolytic streptococci. April 13, 1923, the patient was given 37 cc. of a 1 per cent mercurochrome solution intravenously. She had no marked reaction other than diarrhea. There was no improvement noted in the patient's condition after the injection of the drug. A severe bronchopneumonia had set in at both lower lobes, and this may account for the poor results obtained from the mercurochrome. April 16, 1923, the patient was given a second dose of 37 cc. of a 1 per cent mercurochrome solution intravenously. Again diarrhea was the only effect attributable to the drug. Eight hours later the myocardium failed, the patient's lungs filled with fluid, and she died April 17, 1923.

Case XIII.—Mrs. B. G., admitted April 18, 1923. Aged thirty-three years; Para-IV. Last child four years ago. Two miscarriages; last miscarriage two weeks ago. Last period December 8, 1922.

Eleven days ago the patient had a miscarriage. She did not bleed very much, so her doctor gave her some tablets to insert high in the vagina. These were followed by excessive bleeding. Several days later she got out of bed, but had to return to bed on account of chills and fever. The placenta was not expelled until five days after the fetus was passed. On admission the cervis was open, the uterus was soft and the size of a three months' pregnancy. A blood culture taken April 26, 1923, showed no growth. April 29, 1923, the patient was given 100 cc. of polyvalent antistreptococcic serum intravenously. There was no reaction following the injection of the serum. May 3, 1923, the patient was given 37.5 cc. of a 1 per cent mercurochrome solution intravenously. There was a slight rise of temperature and a moderate chill following the administration of the drug. A blood culture taken just before the drug was given was reported sterile. The patient became progressively worse, developed pulmonary edema, and died May 11, 1923.

This case was not really suitable for the proper use of mercurochrome

because of the sterile blood cultures and absence of definite signs and symptoms of a blood-stream infection, and consequently ought not to be considered as a failure in compiling statistics on the intravenous use of mercurochrome.

Case XIV.—Mrs. A. V., admitted June 18, 1923. Aged forty years; Para-VI. Last child born twelve days ago. No miscarriages. The patient was delivered at home by a midwife. Three days later she developed chills and fever. She vomited frequently. On admission her abdomen was much distended. Her vagina and perineum showed extensive lacerations and were badly infected. The cervix was open and the uterus quite boggy. The diagnosis on admission was septicemia, bronchopneumonia, phlegmasia alba dolens, and conjunctivitis. A blood culture taken on admission showed hemolytic streptococci. June 25, 1923, the patient was given 25 cc. of a 1 per cent solution of mercurochrome intravenously. There was no reaction from the drug; the patient was *in extremis* at the time of its administration, and died the following morning.

Case XV.—Mrs. J. N., admitted July 1, 1923. Aged thirty years; married eleven years; Para-III. Last child born ten years ago. The patient had a miscarriage one year ago. Her last period was April 26, 1923. The patient was about two months pregnant. Two days before her admission to the hospital she began to bleed, and continued to bleed until evacuated two days after her admission. She insisted that the abortion was spontaneous. On admission her temperature was 103.6° F., pulse 128, and respiration 33. The patient ran a typical septic temperature, so a blood culture was taken July 3, 1923, and later reported positive for Streptococcus hemolyticus. July 4, 1923, the patient was given 30 cc. of a 1 per cent mercurochrome solution intravenously. There was a fairly good reaction to the drug and the patient appeared to be somewhat improved. A blood culture taken two days later was reported sterile. July 9, 1923, smears were taken from the patient's mouth, which was badly infected. These smears showed many spirilla of Vincent and many fusiform bacilli. July 18, 1923, another blood culture was taken and later reported sterile. The patient ran a subnormal temperature but appeared to be clinically improved. Her appetite was good and she did not appear toxic. July 21, 1923, the patient became listless and semistuporous. She grew steadily worse and died July 24, 1923.

In this case the blood stream was successfully sterilized by the intravenous use of mercurochrome, but the patient's vitality had been so reduced by the infection that she had no reserve and was unable to combat the oral infection, anemia, etc., which later caused her death. This case illustrates the necessity for early use of the drug before the patient's constitution has been too greatly undermined by the infection.

Case XVI.—Mrs. M. K., admitted December 4, 1923. Aged thirty years; married two years; Para-I. Menstrual history normal. Last period

March 7, 1923. The patient was admitted in active labor. Her membranes had ruptured spontaneously two days before labor pain began. She had a short, easy labor and was delivered spontaneously of a living female child. The patient was examined only once, and then in the hospital, after careful cleansing and under strictly aseptic conditions. Three days after delivery she developed a high fever. The lochia was very scanty. The patient was put in the Fowler position and liquids were forced. The temperature did not drop in forty-eight hours, so a dilatation and evacuation of the uterus was done and a portion of placenta removed. The uterus was douched with diluted hyclorite solution. There was a temporary improvement following this, but after two days the temperature rose again. December 18, 1923, a second dilatation and evacuation of the uterus was done. A blood culture taken December 14, 1923, was reported positive for hemolytic streptococci. December 25, 1923, the patient was given 25 cc. of a 1 per cent solution of mercurochrome intravenously. She had a very good reaction to the drug and was clinically improved. December 31, 1923, a second blood culture was taken and the patient given 30 cc. of a 1 per cent solution mercurochrome intravenously. She again had a very good reaction and her temperature dropped somewhat. The blood culture was subsequently reported sterile. January 17, 1924, a third blood culture was taken and the patient was given 40 cc. of a 1 per cent solution of mercurochrome intravenously. Her temperature then dropped and stayed down for two days. The blood culture was reported sterile. The patient then developed thrombophlebitis in the right leg. This finally suppurated and was opened and drained February 16, 1924. A large amount of pus containing long chains of streptococci was discharged from the abscess, and healing was very slow, due to the patient's weakened condition. The leg finally healed and the patient was discharged in good condition April 17, 1924.

Case XVII.—Mrs. A. C., admitted January 17, 1924. Aged thirty-seven years; married seventeen years; Para-VII. Last child born January 13, 1924. The patient was delivered of a living child January 13, 1924. She was attended by a midwife, but had a short labor and spontaneous delivery. About two hours after delivery the patient developed a severe pain in her left lower abdomen. That night she had a severe chill. She passed a number of clots until January 17, when the lochia stopped and she had another chill. On admission the patient was running a high fever and appeared quite toxic. There was marked tenderness and a mass in the left adnexal region. A blood culture taken January 17, 1924, was sterile. The patient had a moderately severe bronchopneumonia and left-sided pleural effusion. February 12, 1924, after the lung condition had cleared up, the patient was operated on, and a densely matted mass of adhesions to the pelvic organs and intestines separated. A large ovarian abscess was found on the left side and left salpingo-oöphorectomy done. A partial hysterectomy had to be done on account of the necrotic condition of the uterus. The pelvis was drained and packed with gauze. The patient continued to run a septic temperature following the operation.

A blood culture taken January 29, 1924, was sterile. Another blood culture was taken February 15, 1924, and later reported as showing Staphylococcus albus. February 19, 1924, the patient received 25 cc. of a 1 per cent mercurochrome solution intravenously. She had a moderate chill and marked diarrhea following the administration of the drug. Her temperature dropped somewhat and she seemed clinically improved. February 26, 1924, another blood culture was taken and a second intravenous injection of 30 cc. of a 1 per cent solution mercurochrome given. This blood culture was later reported sterile. The patient had a very marked reaction to this dose of mercurochrome. Her temperature dropped to normal and stayed there. In the meantime the patient developed a fecal fistula through which was passed most of the food ingested. Accordingly, rectal feeding was resorted to and some improvement was noted. April 11, 1924, the patient developed a large abscess in the right buttock. This was opened and drained, and from this time on the patient has continued to improve. She made a complete recovery and was discharged.

From the foregoing cases it can be seen that the intravenous use of mercurochrome is not a cure-all, and it must be clearly understood that its use is not entirely without danger. Its use should, at present, be strictly limited to hospital practice, where emergencies may be treated as they arise and where proper and frequent laboratory tests may be carried out. If this is done, and the condition of the kidneys and gastrointestinal system carefully watched, the drug may be used quite safely and with no untoward effects on the patient. Although the drug has failed in a number of cases, it has undoubtedly been the means of saving the lives of patients who would otherwise have died, and as such must be looked upon as a distinct advance in the treatment of puerperal septicemia.

Summary. During the past four years we have used mercurochrome intravenously in the treatment of 17 cases of puerperal sepsis with septicemia. Of these 17 cases, 7 have been permanently cured. The remaining 10 patients all died. Included in these 10 deaths are 5 patients who were moribund before the drug was used and who were expected to die regardless of any treatment that might have been instituted. In another case no blood-stream infection could be demonstrated, and the mercurochrome was, in a sense, ill-advisedly used. The remaining 4 cases must be classed as failures of this method of treatment, as the condition of the patients at the time treatment was instituted was such that a successful outcome should have resulted.

Whether or not a clinician should determine to use this method of treatment at the present time should be based largely upon his

personal experience. There is undoubtedly a disposition on the part of practitioners to defer the use of this treatment, trying everything else first. It is unfair to apply any method of treatment to a moribund case and then attribute the death of the case to the treatment used.

The following facts may be deduced from a study of these cases:

Chemical disinfection of an infected blood stream is possible. Localized infections, such as pyelitis, can be favorably affected by the excretion of an antiseptic injected into the blood.

Remission of symptoms is observed during the period that blood cultures are negative.

For the first time chemical disinfection of the blood is put on a scientific basis, as to dosage, dilution of the disinfectant in the blood necessary to make it a bactericide, administration, and subsequent management.

What will be the ultimate results of these laboratory and clinical experiments by Dr. Piper in reducing the mortality of blood-stream infections must be determined by a collective investigation.

So far, what has been demonstrated to be possible should encourage a further and larger trial of this method.

# ON THE INTRAVENOUS USE OF MERCUROCHROME IN SEPTICEMIA AND LOCAL INFECTIONS*

By ALFRED STENGEL, M.D.

The demonstration by Piper that the intravenous use of mercurochrome in doses sufficient to sterilize the blood is a safe method of treatment of septicemia constituted a real advance in therapeutics that merits general recognition. Various agents, such as colloidal silver, mercuric chloride, formaldehyde, iodoform and others have been used intravenously, but have been found of no value or ineffective in doses that could be safely administered. When my attention was first called by Piper to the possibility that mercurochrome might be used intravenously in doses sufficient to be effective, I was somewhat doubtful of the safety of so powerful a mercurial, and I believe that Young, who introduced the drug as a local antiseptic, was even more skeptical regarding the intravenous administration. However, upon my suggestion, Piper, with Dr. Thomas McMillan, made a number of tests in animals to determine the least concentration in which the drug acts as a germicide and the range of its toxicity. Satisfied by these tests that mercurochrome may be used intravenously without danger in doses sufficient to act as an effective germicide, he ventured to test its value in certain desperate, almost moribund, cases of blood infection, and demonstrated that it could be used without hazard to the patient in doses that effectually sterilized the blood stream. In these earliest cases, selected on account of their hopelessness, though the blood cultures were sterile after the use of mercurochrome, the patients succumbed. Subsequently, less prolonged and serious cases were treated and elimination of the bacteriemia and recovery of the patients resulted. Convinced by these preliminary investigations, which the type of cases falling under his care made it possible for him to carry out, I felt justified in having him treat some of the cases of blood infection

* Read March 4, 1925.

under my charge, and was soon satisfied that his contribution to practical therapeutics was one of very great importance. The cases first selected in my wards happened to be instances of staphylococcus septicemia—a particularly virulent form of general infection—and the recovery of a seemingly hopeless case of this sort and the almost dramatically prompt evidence of improvement in the patient's condition were, to say the least, convincing.

Up to the present time my experience with general infections has included the following: Staphylococcus, Streptococcus hemolyticus, Streptococcus viridans, gonococcus and typhoid bacillus (?); I have had no experience with colon infection, which some observers apparently have found especially amenable to this treatment.

The most striking results in my experience have been in the staphylococcus cases. In no case of subacute infective endocarditis (Streptococcus viridans) have I seen the slightest benefit, and I have omitted any notes of the five cases of this sort that have been treated with mercurochrome under my supervision.

The most demonstrable effect of the intravenous injection of mercurochrome is the sterilization of the blood stream. It was upon this fact that Piper originally built up his confidence in the method, and it was toward a dosage sufficient to secure this result without overstepping the limits of nontoxicity that he directed his preliminary investigations.

Some of the observations I have made, however, have suggested that the therapeutic results obtained may, in certain instances, be due to a different kind of action than that of a mere germicide. The severe reactions produced by the injections and the remarkable, almost immediate, relief from pain in some of our cases recalled like results obtained from other forms of intravenous treatment attended with violent shocks in which there was no probability of a germicide effect.

Some of the cases in which I have used mercurochrome, with apparently curative effect, have been instances of probable general infection at an earlier stage with local residual lesions at the time of treatment. In these it seemed more likely that the result achieved was due to a nonspecific shock rather than to any germicidal action. One apparent result of the intravenous use of mercurochrome to which Piper has called attention was exemplified by the osteomyelitis cases under my care. The effect of the treatment, seemingly, is a localization or focusing of the infection when the blood stream is

sterilized. This result is attended with marked general improvement in the patient's condition and the fixation of the infection in a local lesion that may then be managed surgically.

I do not regard it as important to discuss the details of treatment or dosage here, as these matters have been sufficiently indicated in Piper's papers.

Cases I to IV in my series were instances of staphylococcus infection, the first two being general blood infections, the third one of possible but not demonstrated blood infection, and the fourth one of somewhat uncertain nature. One other case of severe acute osteomyelitis with general infection and recovery after mercurochrome occurred in my wards, but I have been unable to find the record, which has been misplaced.

Case V was a case in which, on one occasion, a blood culture of Staphylococcus aureus was reported, but in which, on a previous occasion, a hemolytic streptococcus was found in the blood, and later the same organism was recovered from a local suppuration. This case, therefore, is apparently one of streptococcus rather than staphylococcus infection.

Cases VI, VII and VIII were instances of gonococcus infection—Case VI, one involving the blood stream (culture), the other two being marked cases of gonococcus arthritis. In Case VI mercurochrome was apparently efficacious; in the arthritis cases no useful result was obtained.

The cases of streptococcus infection in which I have seen mercurochrome used (except Case V) are not summarized, as the Streptococcus hemolyticus cases were not under my immediate care and will, therefore, be reported by others, while the subacute endocarditis cases gave entirely unsatisfactory results.

The case of possible typhoid infection referred to was a somewhat doubtful one, which, however, seemingly justified the belief that nonspecific shock may be a factor of importance in the action of mercurochrome. In addition to these cases, I have used mercurochrome in a few others of varied character, especially cases of arthritis of uncertain etiology, but I am unable to record any useful results.

My own impression of the value of mercurochrome, based upon personal experience, is that it has great value in generalized staphylococcus infection and, perhaps, in gonococcemia. As these are conditions that are favorably influenced by no other treatment, the

possible value of mercurochrome represents a very great addition to our therapeutic resources.

Case I.—M. R., aged fifteen years; admitted September 28, 1922, on account of severe pains in left shoulder and elbow and right elbow and right knee. The affected joints were swollen, red, and very tender to touch, and the skin over them was glistening. The temperature range for several days after admission was from 99° or 100° F. in the morning to 102° F. in the evening, and on the fourth day, after a chill, the temperature was 105° F. Aside from the joint conditions, physical examination showed marked flushing of the face, a heavily furred tongue, a few rales at the base of the lungs, and a soft systolic murmur over the precordia. There was a punctiform red rash on the lower abdomen. The blood examination showed 26,500 leukocytes with 79 per cent of polymorphonuclear neutrophiles. Under continued use of salicylates or aspirin and codeine, the joint pains lessened, but otherwise conditions were unaltered. The blood cultures taken October 4, and October 6, 1922, showed a hemolytic staphylococcus. Later, the patient's pain increased and his general condition grew worse. On October 15 he was in opisthotonos, had rigidity of the neck and a tache cerebrale, but there was no Kernig or Babinski sign, no evidence of cranial nerve palsy, and, though he moaned and cried constantly, there was no loss of consciousness. On October 18, 1922, a swelling of the left buttock, first noted on October 11 as a redness, was incised, and 200 cc. of pus evacuated. Culture of this showed staphylococcus. A fall of temperature followed the drainage, but the level was only a little lower than before the abscess developed; the other symptoms continued unabated. On October 21, an intravenous injection of 1 per cent mercurochrome was given at 1.10 P.M. A severe reaction with a heavy chill followed. At 6 P.M. there was practically no pain in the joints and the patient's general condition was remarkably improved. All of the joints, except the left elbow, soon became quite normal and there was no further pain.

The blood culture taken October 22 (twenty-four hours aftr the mercurochrome injection) was sterile. Another culture taken December 2, 1922 also showed no growth. On this same date a second injection of 20 cc. of mercurochrome solution was given on account of persistent (through lower) fever and the condition of the left elbow. A sharp reaction followed, and subsequently the patient's general condition continued to improve, though some irregular fever continued and the left elbow remained enlarged and somewhat fluctuating. (The course of the joint changes suggested a focusing of the infection in this one joint.) An *x*-ray examination showed osteomyelitis of the upper third of the ulna. Dr. Eliason operated on November 10. Pus was evacuated and the diseased bone curetted. A communication was found extending into the joint which was full of pus. The blood culture on November 16 showed no growth. The subsequent course of the case was uneventful.

Case II.—P. B., a student, aged seventeen years; admitted February 7, 1923, with headache and myalgic pains; had had a cough for several weeks

and had developed sore throat, headache and fever ten days before admission. The temperature ranged from 100° to 101° F. The throat was congested and both tonsils were enlarged and inflamed. The general physical examination was negative. The blood count showed: Leukocytes, 22,400; polymorphonuclear, 82 per cent. There was pain in the right ear and abscess of external auditory canal on February 8. Later there was a free discharge of pus, but the ear condition subsided in a few days. The right elbow and back were very painful on February 12, and the elbow was swollen. On February 13, the head retracted and the neck was stiff, the knees and ankles were affected. The salicylates were given freely and the joints much improved on February 15. On February 20, there was a distinct systolic apex murmur and on February 23 a pericardial friction. The blood culture was reported as hemolytic Staphylococcus albus. On February 25 Dr. Randall found the right ear drum congested but no discharge. He believed the left tonsil more likely the primary source of the infection. The joint swellings had become more marked and extensive. On February 25 (6 P.M.), 32 cc. of mercurochrome was injected followed by a severe reaction with 3° rise of temperature, and a second chill at midnight. On February 26 the joints and general condition was improved. On February 27, 30 cc. of mercurochrome was injected and slight reaction was followed by improvement the next day. On March 5, there were signs of fluid in the left pleural cavity and possibly also in the pericardial sac, and 150 cc. of clear fluid was aspirated. On March 6, 33 cc. of mercurochrome was injected with a mild reaction, followed the next day by distinct improvement. The blood culture, taken February 28, showed no growth. On March 11, the blood culture, taken March 6, showed slight growth of staphylococcus and signs of possible consolidation of the left upper lobe. There was a gradual defervescence after the last mercurochrome injection. The physical signs in the chest gradually cleared with eventual complete recovery except for the systolic murmur.

Case III.—A. B., aged forty-six years; was admitted December 19, 1923, on account of some headache and pain in his back. His illness began eight months previously with severe headache, and he was treated for ten weeks in another hospital. While there his headache subsided, but the pains in his back and extending down the backs of his thighs developed. There is also a vague account of occasional chills, but no vomiting, vertigo, or delirium. There was no muscular rigidity. A diagnosis of influenzal meningitis was made. After discharge from this hospital he attempted to resume his work, but on November 27, 1923, returned to the same hospital with increased headache and lumbar pain. There was now some fever (about 102° F.), which continued up to December 1, after which it was absent up to the time of his discharge. A lumbar puncture made December 1 showed normal pressure and 3 to 5 cells. A second lumbar puncture on December 3, showed slight increase in cells and a few Gram-negative diplococci. There were no significant signs of meningitis at this date. He was discharged at his own request December 12, 1923.

On December 19, 1923, he was admitted to the University Hospital.

The patient had stayed in bed at home and had grown progressively worse. No additional information of importance was obtained in his previous medical, social, or family history. The patient, on admission, was manifestly very ill—stuporous, cyanosed, and with leaky skin. The teeth were in very bad condition. The neck was markedly rigid. There was definite Kernig and Babinski on both sides and tache cerebrale. The extremities were flaccid and the deep reflexes were greatly diminished. The leukocytes numbered 22,000. The bladder was distended and 400 cc. of urine were drawn by catheter.

Lumbar puncture was made December 20, and a very thick greenish stringy pus washed out with salt solution. About 20 cc. of pus was removed and 15 cc. of antimeningococcus serum introduced. Six hours later cisterna magna and lumbar puncture were performed simultaneously. The cisterna fluid was only slightly turbid but under great pressure. There was a complete block below and no fluid could be obtained from the lumbar puncture needle. Forty cubic centimeters of fluid was removed and 30 cc. of antimeningococcus serum was injected at the cisterna. The pus from the lumbar puncture showed Gram-positive cocci on smear. The culture showed luxurious growth of staphylococci. The cisterna fluid showed 3240 polymorphonuclears, 64 mononuclear cells, and 140 red blood cells. The smear showed Gram-positive cocci. The culture showed hemolytic Staphylococcus aureus. On December 21 a double puncture was again performed; the canal was still blocked and mercurochrome (20 cc.) was given intravenously. On December 22, the cisterna was drained and washed; the lumbar region could not be washed. On December 23, by cisterna puncture, 30 cc. of a uniformly bloody fluid, under low pressure was removed. On December 24, "There seems to have been a general improvement since the injection of the mercurochrome, the stupor is less marked, the pulse of better quality and the fever lower. The signs of meningitis persist. The temperature was normal all day. The patient can coöperate well now and is much brighter than on admission."

On December 27, 1923, on account of a slight return of fever (100° F.) 16 cc. of mercurochrome was injected intravenously. On December 30, the rigidity of neck had disappeared, the deep reflexes were all present and, more decided, there was a little return of fever in the afternoon. On December 31, mercurochrome (30 cc.) was injected intravenously followed by considerable discharge of pus from the site of the lumbar punctures; better drainage was required. On January 6, 1924, the drainage tract was enlarged and probed; there was no definite evidence of osteomyelitis; an ounce of pus was released and the wound washed and packed with mercurochrome gauze. On January 8, mercurochrome (25 cc.) was injected intravenously. On January 10, Dakinization of the wound. On January 18, the patient was transferred to the surgical division, the wound opened and Dakin tubes sewed in place. After long-continued care in the surgical ward the patient was discharged in good condition May 6, 1924.

Case IV.—E. K., aged twenty-four years. Referred by Dr. A. S. Weiss, Lebanon, Pa. Five years previously, after a partial tonsillectomy, he had

a persistent swelling with blueness and pain in the right foot. Various treatments, including vaccine from tonsil culture, were ineffectual. Recovery followed removal of an abscessed tooth.

In July, 1923, after a slight injury to the little toe of his left foot and following a second tonsillectomy, the left foot, and later the knee, became swollen and very painful There was irregular fever up to 101° F., and the patient was bed-fast for eight weeks. Heat, fixation, supportive treatment and vaccine from the tonsil culture did not help his condition materially. There was great loss of weight and the patient's general condition was unsatisfactory. An *x*-ray study of the knee and ankle was reported as showing a tuberculous condition. Dr. A. P. C. Ashhurst did not concur in this opinion, but regarded the evident disease of the upper end of the tibia and fibula as a chronic osteomyelitis, probably due to staphylococcus, the organism obtained from the tonsils.

When seen by me January 16, 1924, the conditions remained much as described, though there was no longer fever nor quite the same pain and swelling of the knee as formerly. Upon my recommendation, Dr. Weiss gave two intravenous mercurochrome injections (20 cc. and 30 cc.). After recovery from the sharp reaction following the first injection the patient began to improve immediately, and after the second injection, a week later, the reaction was even more severe, but further improvement became manifest. At the time of the last report Dr. Weiss states that "the fibular lesion seems to have disappeared entirely, while the tibia has improved about 75 per cent." A third injection was advised.

Case V.—E. W., aged twelve years, admitted November 17, 1922; discharged February 23, 1923. Chief complaint painful joints. For six he had eczema and boils in the right external auditory canal. Eleven days before admission he had swollen glands below right ear. Five days before admission an incision was made under gas anesthesia at the Howard Hospital by Dr. Bates and no pus found, but gray, partly necrotic gland. The patient was unimproved, with continued high fever. Two days before admission there were painful red swollen joints on the right hand, right elbow and knees. On the day before admission he was seen in consultation by Dr. Kern, and a clinical diagnosis of septicemia with secondary joint manifestations was made. Referred to University Hospital. (This record is included by courtesy of Dr. Richard A. Kern.) The previous medical, family history and social history were all negative.

*Physical Examination.* Painful, swollen, tender joints. Skin hot and dry. Draining sinus right side of neck. Lungs clear; heart rapid, but sounds normal. Spleen not enlarged. No petechiæ.

The temperature on admission was 101.8° F., pulse, 128; respiration, 28. On November 18, 1922, red blood cells, 4,060,000; hemoglobin, 70 per cent; white blood cells, 14,000; polymorphonuclears, 85 per cent. On November 19, the blood culture of November 17 was reported positive hemolytic streptococcus and 50 cc. antistreptococcus was given intravenously. On November 20, 50 cc. antistreptococcus serum was injected intravenously, followed by marked reaction—chill, fever, urticaria; the joints were less

painful; white blood cells, 13,300. On November 21, 50 cc. antistreptococcus serum was injected intravenously; reaction—chill, fever, urticaria. On November 24 the patient's condition was not improved, the temperature varied between 100° and 104.2° F., and the white blood cells numbered 12,200. Mercurochrome, 20 cc. of a 1 per cent solution was injected intravenously, followed by chills. On November 27, there was a wide temperature fluctuation, the temperature reaching normal in two days. Twenty-five cubic centimeters of a 1 per cent solution of mercurochrome was injected intravenously followed by a severe reaction, the temperature rising to 106.4° F. There was no bowel movement until fifteen hours after the drug, and then as a result of an enema. On December 1, the blood culture taken November 27, before the mercurochrome injection, was reported positive hemolytic Staphylococcus aureus. For over a week the tenderness gradually increased, being most marked in the upper end of the femur; the *x*-ray was negative. The daily temperature curve was lower. On December 12, the blood culture taken December 9 was sterile. On December 23, there was continued irregular fever, with tenderness sharply localized in the left upper femur.

*X-ray.* Bone changes were found in and around the hip-joint. On December 27, operation for purulent osteoperiostitis and arthritis of left hip was done by Dr. Eliason. The culture was hemolytic streptococcus. The subsequent convalescence was uneventful and the patient was discharged cured on February 23, 1923.

Case VI.—E. S., a young woman, aged twenty-seven years; admitted October 28, 1922, on account of chills, fever, and headache. In June, 1922, the patient had a chill followed by fever in the righ knee and later in several joints. In March the patient had noted a vaginal discharge with burning and frequency of urination.

On admission she was found emaciated and had papules and pustules in various parts of her skin surface. Pelvic examination showed inflamed Bartholin's glands, a purulent urethral, vaginal, and a cervical discharge. The right knee was still somewhat painful but not swollen. The blood count showed 34,400 leukocytes. The temperature on admission was 101° F., that evening it rose to 104° F., and then rapidly fell to normal. After two days of normal temperature the patient had a chill and recurrence of fever (reaching 105° F.). Another crisis, nearly to the normal, occurred on the same day, and a second chill with elevation of fever to 105° F. Again a critical decline to normal during the night, after which there was a normal temperature during nine days, when a chill and fever ($105\frac{3}{5}$° F.) again occurred. Subsequently, similar attacks were seen at varying intervals, the temperature being normal between paroxysms. One doubtfully positive Wassermann test was reported on October 28, and a negative one on January 5, 1923. Gonococcus-fixation test was positive, and Gram-positive intracellular diplococci were found in the urethral pus. A positive culture of gonococci was reported on November 27, 1922.

It was of interest that some of the chills and high fever followed after the vaginal examinations. No local lesion of the adnexa was ever discovered in the repeated examinations.

On December 2, 1922, 20 cc. of mercurochrome was injected. Some of the fluid escaped into the tissues of the arm and caused considerable soreness and swelling. The patient subsequently improved steadily, and was finally discharged from the hospital January 13, 1923, decidedly improved.

Case VII.—M. C., aged twenty-two years; admitted November 12, 1923, with pain and swelling of the right foot. Specific urethritis began in September and the condition was untreated. On November 2, 1923, pain and swelling of the right foot were noted. The pain became very severe and interfered with sleep. On admission there was marked pain, swelling, and redness of the right foot. There was still an active urethral discharge, and some enlargement of the prostate was also present. The pus contained gonococci. Gonococcus vaccine treatment was first used without discoverable benefit; later, intravenous injections of typhoid vaccine; and finally, on February 4, 1923, 25 cc. of mercurochrome were injected. But there was no clear evidence of improvement as a direct result of any of these treatments. The symptoms, however, were ameliorated, and he was discharged improved on February 8, 1923.

Case VIII.—J. K., aged twenty-four years, admitted March 3, 1923, with pains in both knees and heels. He had purulent urethral discharge a month before. A week after onset, pain began in the heels and subsequently in knees. General stiffness was also noted, and the knees were quite swollen and tender. There was an active urethral discharge, which showed intracellular diplococci. There was moderate fever.

Aspiration of the knee-joints gave a certain amount of relief. Later, mercurochrome injections were given (20 cc. and 25 cc.) on March 5, and March 9, 1923. In each case there was a distinct reaction, especially after the second, and following the latter acute bilateral parotitis developed. No distinct improvement in the arthritic symptoms followed, and intravenous injections of 25,000,000 typhoid organisms were given on April 2, and April 9, 1923. Though no immediate effect was observed, improvement followed the second injection, and the patient was discharged May 9, 1923, practically well.

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## DISCUSSION ON THE PAPERS OF DRS. HIRST AND STENGEL

Dr. Edmund B. Piper: Some days ago an officer of the College stated to me that he hoped in my discussion this evening I would not become too enthusiastic over this method of treatment. He further stated that in all the cases of which he had knowledge, in which recently I had been called in consultation, there had been uniform results, that is, the patients all died. I am forced to admit that in so far as the doctor had information he is quite correct, but there were one or two about which he had no knowledge that, strangely, recovered. However, I am sure that this friend of mine can have no complaint that I am overenthusiastic.

At least one of the speakers tonight stated that he had encountered no dangerous symptoms from the use of the drug. I am sorry to say that in three cases I have seen anuria follow its intravenous use. I believe it is dangerous when used when there are definite contraindications and when used with improper technic. Opium used before the intravenous administration should at least be used very guardedly. Symptoms of acute nephritis should be looked on as a definite contraindication. The administration of the drug to a clearly moribund case, and expecting that moribund case to eliminate normally, is unreasonable. When used in a case of this kind it should be looked upon as a last resort and I believe it to be unfair to credit the death of the patient to the use of this drug.

For a working hypothesis of the action of mercurochrome intravenously, in order to explain the sharp reaction that occurs, I have assumed that if it acts as a germicide it creates within the blood stream a situation analogous to the injection of a massive dose of autogenous vaccine. I do not mean to assume that the chill reaction and all that goes with it are due to that alone, but I believe it to be a combination of the injection of a foreign protein, of mercurial poison and the release of the endotoxins or dead bacteria.

Recently a doctor asked me to see a case of puerperal septicemia. He said that four days previously they had got a positive blood culture. Subsequently he had asked a colleague of mine to see the case and this colleague had suggested that he ask me to see it. I remarked to him that if this particular colleague (a close personal friend) asked me to see the case, she was probably ready to die. I did not see her, but she died in twenty-four hours. I merely state this to illustrate the fact that very frequently we are not asked to see these cases of puerperal septicemia until they are much too mortally ill for any efforts to be of avail.

This treatment was originally evolved for use in puerperal septicemia, and as has occurred in many therapeutic measures it has been shown to be of much greater benefit in other conditions. In fact, I am inclined to think that in all the conditions in which I have had occasion to use this method the results of puerperal septicemia appears to be the worst. The reports I have had when used in the complications following mastoid operation in children seem to be the best. There is a basic principle in surgery that should be constantly born in mind, and that is that no blood-stream infection may be cured where there is a focus which is not properly surgically drained, whether the focus is primary or secondary. Our good results have occurred in those cases which have been carefully watched medically and operated surgically at the proper time. The proper draining of local collections of pus is of primary importance.

In concluding, I wish to emphatically state that, although this method of treatment has cured cases which in my opinion and that of others would otherwise have died, I do not believe that it is the answer to blood-stream infection. I believe there is something that is the determining factor in the recovery or fatal termination of blood-stream infections that up to the present is unknown. Our bacteriological friends may some day show us what this is, and although I do not think the intravenous use of mercurochrome is a failure, neither do I believe it to be an unqualified success.

Dr. John A. Kolmer: Naturally we have been very much interested in the observations reported this evening on the clinical results following the intravenous administration of mercurochrome in the treatment of a variety of bacterial infections. The subject is of special interest because the chemotherapy of bacterial diseases offers today a very interesting, important and probable fruitful field for scientific endeavor. Up to the present time most accomplishments in chemotherapy have been in the protozoal and metazoal diseases, but the great field of bacterial infections awaits future discoveries. I have employed mercurochrome somewhat extensively both in laboratory infections and in the treatment of a number of human beings. My laboratory work, largely conducted with the assistance of Dr. Malcolm J. Harkins and Miss Anna Rule, has been confined to experimental streptococcus and staphylococcus septicemia of rabbits and rats and of meningitis of rats and guinea-pigs. In a general way, I feel that maximum doses of mercurochrome by intravenous injection may occasionally influence favorably an otherwise fatal streptococcus and staphylococcus septicemia of these animals, but our results have been somewhat irregular and in no instance have brilliant results been observed. I hasten to add, however, that our experimental infections have been usually very severe, and doubtless better results could be observed with less severe and less rapidly fatal infections. For example, when mice are employed, infected with streptococci by subcutaneous injection after Morgenroth's method, the results have usually been better.

Laboratory and clinical experience have led me to the opinion that the intravenous administration of mercurochrome, in dose of 0.005 gm. per kilogram of weight, unquestionably at times removes organisms from the blood stream, at least temporarily, but, so far, I have had no evidence of this compound being able to penetrate and disinfect local areas of infection. On the whole, I regard the introduction of mercurochrome as an additional means for combating septicemia and particularly that produced by the streptococcus and the staphylococcus.

But this drug should not be used as a substitute for other well-established methods of treatment; rather it is but a useful adjuvant in some cases. For example, it does not remove the necessity of surgical drainage when this is possible; in my experience, best results have been secured by using the drug in conjunction with drainage and biologic forms of treatment. For example, I have had best results in the treatment of streptococcus infections by employing mercurochrome along with antistreptococcus serum, and sometimes with blood transfusion, and especially the transfusion of large amounts of blood, like 800 to 900 cc., instead of repeated small transfusions.

Clinically I believe that mercurochrome is especially useful in cases of staphylococcus septicemia, and particularly since in this infection we do not have an efficient serum-therapy. I have had a few apparent very successful results along, however, with some disappointments, and notably the apparent inability of the drug to influence the staphylococcus septicemia which proved fatal for the son of President Coolidge.

In my experience with 3 cases of endocarditis caused by Streptococcus

viridans, mercurochrome was without beneficial influence in so far as the valvular lesions were concerned. In 1 case I gave as many as eleven intravenous injections, but without a successful outcome. In this manner my experience corresponds with that reported this evening by Dr. Stengel. I may also state in this connection that the intravenous injection of mercurochrome apparently fails to sterilize apical abscesses of the teeth, which in 2 of my cases were the foci of primary infection. Even after three doses of the drug the extraction of three teeth in 1 case was followed by overwhelming blood infection, ending fatally in about thirty-six hours.

So far I have not observed any particular toxic reactions. I have had no evidences of nephritis or severe gingivitis, 1 of my cases, however, developed severe ileocolitis. I may state, however, that, since mercury is highly renotoxic, the drug should not be given at all or at least not in the maximum dose when there are evidences of nephritis. Albuminuria due to hyperpyrexia, however, in my experience, has not become worse under mercurochrome therapy.

In my opinion a great problem of chemotherapy in the treatment of bacterial infections is the discovery of a chemical agent capable of penetrating and disinfecting local foci of infection. I doubt that mercurochrome has this property, and for that reason I would not expect it to favorably influence lobar pneumonia unless it be by disinfecting the blood and reducing the chances of hematogenous metastases in this disease.

Dr. Hare has suggested for discussion the matter of affinity of mercury for the kidneys. I believe that toxic nephritis by mercury is the result of the influence of the mercury ion upon the tubular epithelium, and that the renotoxicity of mercurial compounds will vary according to the degree of ionic dissociation occurring before or during elimination. Mercurochrome probably belongs to the half complex or pseudocomplex organic mercurials, in which the compound may be eliminated in part before dissociation occurs. This may account for the fact that this compound is less toxic for the kidneys and other organs of elimination, and notably the liver and gastrointestinal mucosa, than compounds more rapidly dissociated, like mercuric chloride.

Dr. Jay F. Schamberg: I should like to emphasize the implied caution of Dr. Piper when he stated that he had seen some untoward effects from the use of mercurochrome. I believe that the tolerance of different patients to mercurochrome varies. A patient suffering from pemphigus, treated in the Polyclinic Hospital by my associate, Dr. Greenbaum, received 5 mg. per kilo of a 1 per cent solution of mercurochrome. This was followed by persistent vomiting, complete anuria and death within twenty-four hours. Dr. Hugh Young, of Baltimore, with whom I later discussed this case, seemed to think that this was not a mercurochrome death. In view of the fact that the man's general condition appeared to be excellent before the treatment, it would seem to me that it would be difficult to absolve the drug from having induced a fatal outcome in this case. One cannot be guided entirely by the amount of the drug which is tolerated in small

animals, as the larger the animal the smaller the dose that can be tolerated in milligrams per kilo. Bichloride of mercury is tolerated in the white rat in about 2 mg. per kilogram of body weight in terms of the mercury content. Mercurochrome is tolerated in about 50 mg., but as this drug contains little over 20 per cent of mercury, it would seem that its toleration was about five times that of bichloride of mercury. It is possible in the laboratory to produce a number of mercurial dyestuffs, some of which are less toxic in the experimental animal than mercurochrome. Many of the products of low toxicity also have a low therapeutic effect, whereas, on the other hand, some of the products with relatively high toxicity have a better therapeutic effect and a superior therapeutic index. I do not believe that it is always essential to use high doses of mercurochrome to produce good therapeutic effects, nor do I believe that it is necessary to induce a reaction. I have had several brilliant results in local infectious conditions and in mild bacteremias with extremely small doses, for instance, 5 cc. of a 1 per cent solution. We cannot expect that mercurochrome will act equally well against various organisms or, indeed, against different strains of the same organism in the blood. We do not yet know what its biochemical affinities are. Its clinical uses will have to be defined by further experience. I have no doubt that other compounds will be elaborated which may perhaps be successful in the treatment of those cases which are resistant to mercurochrome.

Dr. Young and his associates are to be congratulated on the elaboration of this very interesting and valuable compound, and Dr. Piper is to be felicitated on the application of this drug to bacterial blood-stream infections. Work of this kind constitutes a confirmation of the principles of chemotherapy originally advanced by Ehrlich. It seems to me that the outlook for the future is most hopeful along this line of development. This field constitutes a most fertile domain for further therapeutic investigation.

Dr. William R. Nicholson: I have been very greatly interested in this work since Dr. Piper began the use of mercurochrome intravenously, but I feel that it is necessary always to remember that there is a decided danger in its use. Until we know more about it I do not think that this method is at all applicable in the ordinary case of sepsis. I mean until all other usual methods have been tried.

Since Dr. Piper's work has become so well known I have been appealed to to allow its use in cases which subsequently turned out to be simple sapremias. This is no argument against Dr. Piper's method, since his indications for its use are always based upon suitable scientific study; but it simply shows that the profession in general has not realized that this treatment has possibilities for evil which cannot be disregarded.

Dr. Piper and I have seen 1 case of sepsis become anuric within a few hours after the administration of this drug. This woman would have died in any event. She had only been delivered three days before and yet she was almost moribund when I saw her. She had a positive streptococcic blood culture and her condition was so desperate that we felt justified in giving her the mercurochrome as a last resort. She developed a marked

reaction and really improved decidedly for a few hours. Her kidneys then ceased to function and she died with complete suppression.

I think that cases such as these should be reported in order that the general profession can realize that they are dealing with a very dangerous remedial agent.

Dr. Stengel (closing): I agree with Dr. Nicholson in the last remark he made and wish to correct Dr. Piper's impression: I did not say that I have never seen mercurochrome do any harm. As a matter of fact, in 1 case in which I advised its use I believe it did do harm; that was a case of Streptococcus viridans infection. It was the impression of the administrator of the drug that it did do harm, but the patient's condition was very serious. I can easily conceive that harm might come in some cases from this drug, and certainly, in the doses we have been advised to give and which we have given, it is not a drug to be administered with absolutely free hand or with any feeling that it is incapable of doing harm. I may say that in cases that were not desperately ill, that is, in patients in whom I felt it unfair to take a larger chance, smaller doses were used than in the more serious cases. In the arthritic cases smaller doses were used than the maximal ones employed in blood-stream infection. How this drug acts and why it acts and whether it penetrates pathologic lesions is for the future to say. I think we know very little about it now.

# FIFTY YEARS IN THE PRACTICE OF MEDICINE.*

By E. E. MONTGOMERY, M.D., LL.D., F.A.C.S.

The progress and development during the last fifty years in every department of business and science has been unexampled in any similar period of the world's history. The telephone, the application of electricity to transportation, lighting, heating, scientific and mechanical arts were then unknown; coal oil for lighting had but recently come into use; the employment of gasoline for promotion and propulsion was a consideration for the future; the wireless, the radio, radium and the employment of the various forms of light were yet uncovered in the land of dreams.

When the physician contemplates the discoveries, now considered necessities, in other lines of human endeavor, he is constrained to ask himself whether his own profession has kept apace with such steps of progress.

The writer, on July 5, 1871, entered the office of the leading surgeon of his native town, Newark, Ohio, to read medicine for a year, as was then the custom, preliminary to study in a medical college. He found but one medical book later than 1848, the year of his preceptor's graduation. As he had no ambition to qualify as an antiquarian, nor desired then to lay a basis by which to determine the progress in medicine, he immediately invested in the latest textbooks. His acquisition of medical lore outside that obtained from his books was scant. He had an opportunity to hold a child undergoing the operation of tracheotomy, without anesthetic, for the removal of a grain of corn from the trachea. This operation was performed by the noted surgeon, W. D. Hamilton, of Columbus, Ohio.

The latter part of August, 1872, the writer came to Philadelphia to attend lectures. It was his first visit to a large city. He found it paved with cobblestones, its traffic was in horse-drawn cars and the

* Read April 1, 1925.

boarding-houses were neither palatial nor inviting. The water for drinking and bathing was pumped and supplied directly from the Schuylkill River, which was the drainage canal for the cities up-stream, and as the cemeteries within the city limits lined the banks on either side, it might be truly said that its citizens acknowledged the virtues of their living ancestors and drank those of the dead. Frequently upon drawing a bath, the indulger would debate whether he would be as clean after as before he had taken it.

The course of instruction in the medical college consisted of lectures given to the two classes in common. A repetition the second year in all but the chair of practice, whose occupant covered his subject in two years. The observing student of the second year knew just how each subject would be presented, even to the time for the introduction of the jokes. The only laboratory was the dissecting-room, upon which neither prolonged nor systematic attendance was obligatory. Both the ambitious student and the one who dreaded the final examination depended largely upon extra-mural teaching for instruction. Among the teachers, our oldest fellow, Dr. W. W. Keen, was the most noted, and his Philadelphia School of Anatomy was highly appreciated and well-patronized by the students of both Jefferson and the University.

The former institution, which the writer attended, numbered in its faculty some of the most-noted members of the profession. Its professor of anatomy, Dr. Joseph Pancoast, of whom student tradition said, could operate successfully for conditions where the patients were sure to die in the hands of others, would say to his classes: "Gentlemen, I cannot tell you why it is, but when I wash a wound with a solution of bichloride of mercury, it heals by first intention."

The professor of surgery, then sixty-seven years old, commended laudable pus, decried the aspirator and discarded the Esmarch bandage. The most of the surgeons of that day prided themselves on their ability to operate without soiling their cuffs and carefully washed their hands after, rather than before, operating.

The professor of obstetrics was cleanly. He persistently urged careful washing of the hands before examination of the patient; but as the latter and the introduction of the catheter were to be done without exposure of the genitalia, the purpose of the cleanliness might be considered to have been defeated. In diseases of women the examination of the genital tract was digital, without exposure,

followed by the introduction of a tubular speculum, around the external end of which the enveloping sheet was carefully drawn. The next step was the introduction of the sound, and if this instrument was not properly curved he would bend it with his teeth. When expressions of disgust were made by the students, he would impress them with the necessity of having the instrument so clean that they need not hesitate to put it into their mouths. Today we would question its fitness for use after the physician had removed it from his mouth.

The chair of practice was newly occupied by Prof. J. M. Da Costa, who began those marvellous clinics on diagnosis which made his name renowned and respected the world over.

The professor of materia medica, Dr. John Biddle, would be popular with many today, as he advocated alcohol as a specific in typhoid fever.

The candidate for graduation was expected to have spent three years in the study of medicine, the first year in the office of a preceptor and two courses of lectures, each six months in length. But one examination was required and that at the end of the second year in college. This examination was oral, and although the students were in a panic when the period for it had arrived, it was easy to pass and difficult to fail.

Some graduates, realizing their incompetence to trifle with life, sought hospital experience. The writer, through the intervention of Dr. R. J. Levis, secured the position of official substitute (a new position) to the Philadelphia Hospital. An examination of the candidates for interns was required before a committee of the staff, but the report carried no weight against political pull. The nurses were the more intelligent paupers or, more frequently the less intelligent who had political influence. In spite of these handicaps the institution afforded a wonderful field for observation. No glimmerings of aseptic or antiseptic measures had apparently yet reached the members of its staff; at least not enough to affect their practice. It is true that Lister had practised antiseptic surgery with marvellous results. White, in 1891, quotes Lister's experience in Glasgow, in 1864–66, when under nonantiseptic methods his mortality was 45.7 per cent, and contrasts this with his work in Edinburg, 1871–78, where in 553 grave cases the mortality from septic diseases was but 0.36 per cent while Spence, in the same hospital, who declined to practice antiseptic methods, had a mortality from sepsis of 2.4 per cent, eight times that of Lister.

What opportunities were dawning for practitioners of surgery? Is it surprising, however, that American surgeons should have been slow in the adoption of methods which were discountenanced and the results doubted by the immediate confrères of their advocate? As usual, truth sooner or later prevails, and the surgeons of the entire world were the gainers by the courage and persistence of one man. Every department of surgery was enriched and made safer by the practice of antisepsis and its subsequent simplification in asepsis. Compound fractures, gunshot injuries and hospital gangrene were no longer the dread of surgery.

It is interesting to observe how the same or similar ideas impress workers in different parts of the world. Thus, in 1872, Battey in this country, Tait in England and Hegar in Germany advocated the removal of the ovaries, but each for a different reason: Battey, to bring about cessation of menstruation when the function was attended with such pain as to completely incapacitate the individual for the enjoyment of life; Tait where the tubes and ovaries were the seat of severe inflammatory and purulent conditions, and Hegar to establish the menopause in severe hemorrhages occasioned by submucous myomata. Experience had disclosed that the occurrence of the menopause was not only followed by cessation of the uterine hemorrhage but also by recession of the growths.

The greater safety afforded all operative procedures through the practice of asepsis led to an epidemic of surgery. Some questioned whether the future of the race was not imperiled through the frequency with which the ovaries were removed, and a female surgeon advocated the removal of the male analogues where the possessor had specific disease, but this suggestion was not enthusiastically received.

Emmet added impetus to the wave of gynecic surgery, in 1874, by his description of the operation he had devised for laceration of the cervix, called trachelorraphy, which he had been practising for twelve years, and had at that time performed some two hundred times. He was heard to assert that had he supposed that it would be so frequently and unwisely performed he would have hesitated to make it known.

Appendectomy, truly an American operation, having been first performed by Willard Parker of New York, in 1848, subsequently frequently performed by Morton, Keen, White and others, remained to our Fellow and confrère, Deaver, to render it fashionable and a source of revenue.

Regions of the body which were considered outside the possibility of successful invasion, as the cerebral, spinal and chest, have become legitimate fields for investigation and treatment.

The removal of large ovarian tumors, denominated ovariotomy, is another American operation. It was first performed by McDowell of Danville Ky., in 1809, and after several operations by him fell into disuse until revived near the same time, in 1844, by Atlee of Pennsylvania, Dunlap of Ohio and Clay of England. Atlee bore an unprecedented onslaught of denouncement and criticism, but courageously and persistently continued his course and lived to see ovariotomy accepted as a legitimate procedure the world over. It has been estimated that Spencer Wells, of England, through the performance of this one procedure, has added many thousands of years to the life of woman.

The writer had a practical application of the relation of sepsis to childbed fever, then known as puerperal fever. He passed from the surgical service, where he had a number of cases of erysipelas, directly to the obstetrical wards, and his advent was followed by an outbreak of infection, called puerperal fever. He well remembers the days and nights in attendance upon these victims, and his sense of discouragement and depression when, in April, 1875, three children were left motherless by the deaths of two women. Here, again, asepsis, the outgrowth of the tide which Lister had set in motion, led to the recognition of this disease as a result of infection and demonstrated the means by which it could be avoided.

Then the hospital was the dread of the parturient woman, now it is her greatest safety.

From time immemorial, Cesarean section had been recognized as an occasionally necessary method of delivery. In the early eighties however, it was shown that a woman could be delivered by the horn of a cow with a less mortality than by the knife of the average surgeon. The British obstetricians and their American followers resorted, in all doubtful cases where the dimensions of the pelvis would permit, to the destruction of the child by embryotomy. One general practitioner of Philadelphia claimed the credit of nineteen craniotomies. The writer, was so impressed with the need that the unborn child should have *its* chance for life that he prepared and read a paper before the Philadelphia County Medical Society, February 14, 1883 on, "Is Craniotomy Justifiable?" in which he asserted there were measures affording the child a chance for life

which could be safely employed for the mother. Oettler, in 1870, had reported a woman living who had undergone four deliveries by Cesarean section between 1853 and 1863. Charles D. Meiggs, in refusing to perform a third craniotomy for Mrs. Roelof, was instrumental in securing for her two children by successive Cesarean sections, and she in her riper years had the comfort of seven grandchildren. The mortality was generally regarded as equalling 30 per cent. This was because the obstetrician of that day was influenced by the dictum, "meddlesome midwifery is bad," and allowed his patient to exhaust her forces and become infected by repeated examinations and efforts at manual delivery, before the Cesarean operation was employed. The writer insisted that the attendant should know, in advance of the expected labor, the size and condition of his patient's pelvis, be prepared promptly to employ the proper means of delivery, avoiding the deleterious procedures and thus afford justice to mother and child. He closed the paper with the assertion, "The obstetrician should control events, not be controlled by them." His suggestions were condemned by his contemporaries, but he has seen every proposition accepted as sound doctrine. As predicted, the Cesarean operation is employed with as much freedom and with greater certainty of success than was ovariotomy then. G. M. Boyd, a Fellow, reported in 1914 that he had performed 48 Cesarean sections without a maternal death, and J. M. Martin, of Glasgow, in 1921, presents 51. Thoms, of New Haven, Conn., reported a colored woman who had 4 Cesarean deliveries between May 1918 and November 1921, in the last of which, feeling that she had done her duty, the operator sterilized her.

The removal of the uterus for myomata and cancer marks another step in progress. These were operations infrequently performed fifty years ago and never for cancer. The cervix, as a stump or pedicle, was brought outside the abdominal wound, secured by a clamp or transfixed by pins, and hemorrhage prevented by a rubber ligature below the latter. Baer, a Fellow of the College ligated the uterine arteries, covered the stump with peritoneum, dropped it back, thus permitting the abdominal wound to be closed. Panhysterectomy is the only operation worthy of consideration in cancer of the uterus. It became not infrequently the operation of election in large myomata when the cervix was spread out by the tumor, was diseased, or the seat of previous injury which made its

retention unfavorable for the future comfort and safety of the patient.

The discovery of the *x*-rays by Roentgen, in 1895, was probably the most striking and farreaching revelation of the age. What must have been Roentgen's sensation when he accidentally saw the skeleton of his hand? Did he then appreciate the possibilities of this discovery? That it dawned upon him as a valuable revelation is evident from the promptness, with which he made it known to the medical profession. Its value was at once recognized, and its employment has developed a branch of medicine useful not only in diagnosis but in treatment as well.

A year later Becquerel described the remarkable radiant energy displayed by a sample of uranium, similar in its action to the *x*-rays. Mme. M. Curie found that the radiation from the *salts* of uranium exceeded many times that obtained from the original metal. Their experiments led to the discovery of radium. The separation of radium from pitchblende has been the greatest and most notable contribution made to science by any woman. These two radiant forces blend to facilitate the diagnosis of obscure conditions and certain restoration of health to persons previously regarded beyond relief by human skill. The *x*-rays make it possible for Jackson and his school of bronchoscopists to follow the foreign body to its resting-place in the smaller bronchi. The writer pauses to speak of the last patient upon whom he performed tracheotomy. He had done intubation, using, from want of a better, a tube rather small for the age of the child. Two days later the dyspnea recurred, and not finding the tube in the larynx, feared that it had slipped into the trachea, not desiring to add another, he did a tracheotomy. The patient was relieved, but the tube was not discovered. Two days later it passed through the intestine, having been coughed out of the larynx and swallowed. Today the position of such a tube would be made known by the rays. Thirty years ago a good *x*-ray picture of the hand could be secured by a thirty-minute exposure, now a better one can be obtained in one-hundredth of a second.

The progress of development in fifty years in every department of surgery and in obstetrics has been marvellous; but, valuable and farreaching as they have been in promoting health and saving life, they pale into insignificance when compared with the progress that has been made in internal medicine. Suspicion had long existed that the occurrence of the plague, cholera, malaria, yellow,

typhoid and typhus fevers, scarlatina, measles and syphilis was due to some infective organisms. In 1881, Laveran described some bodies found in the blood of malarial subjects which he called Oscillariæ malaria, which subsequent to the further investigations of Marchifava and Celli became known as the Plasmoidium malariæ. Singularly enough, Dr. Joseph Jones, of Lousianna, had been investigating the blood of malarial victims since 1859, and from his knowledge of the microscopic appearance of the blood, was able not only to say that some stains found upon the clothing of a man accused of murder were not from paint, as he claimed, but blood, and that of a sufferer from malaria. A similar report on some stains on the door of a safe, and the knowledge that the victim of the murder suffered from malaria, led to the conviction and execution of the murderer. This trial took place in 1877, while Laveran's discovery was not made until 1881. He had not, like Laveran, described the blood changes he had observed. Although the most capable pathologists devoted themselves with the greatest enthusiasm to the study of these bodies, it remained a problem how they reached the blood of the victim; this, too, in spite of the fact that the mosquitoes were singing and stinging in all the affected areas, delightedly endeavoring to disclose their part in the tragedy. One could not but think that, if the mosquito could have knowledge of the situation, she would be inclined to exclaim:

"What fools these mortals be."

To follow the researches into the causes of these diseases is as interesting as a romance, and demonstrates that the research worker must be possessed of imagination. It is said that when Ross, in India, was investigating the filaria in the blood, the specimens supplied by one of the natives employed to make collections was much richer in organisms than those supplied by any other. Inquiry disclosed that he was employed during the day and made his collections at night. Ross concluded that the organism, completing its cycle, at night approached the skin, where some suction insect received and transported it to the next victim. The mosquito occurred to him as the insect to be investigated, and his research disclosed a species of the mosquito, the Culex, as the promotor and transmitter. Later, in 1894, Ross was obliged to leave India, as Manson began his investigations as to the medium through which

malaria was transmitted, and suggested to Manson that he investigate the mosquito, and another species, the Anopheles, was found guilty.

Yellow fever was found endemic among the natives when America was discovered. Some parts of the West Indies and the coasts of Central and South America continuously supplied its victims. In 1802, when the French sent an expedition to Haita, 22,000 out of a force of 25,000 men died of yellow fever in six months, and those remaining were too enfeebled to make an effective invasion. The disease became epidemic at times in the coast cities of the United States from Boston to New Orleans. The disease was supposed to be transmitted by fomites, and much dread was experienced during the Civil War that Confederate sympathizers would transmit the disease in infected clothing conveyed through Canada. When Walter Reed went to Havana, to study how the organism of yellow fever completed its cycle, he was already imbued with the inclination to investigate the mosquito, from his knowledge of what had been ascertained by Ross and Manson in their study of filaria and malaria. The particular mosquito was indicated to him by Dr. Carlos Finley, who had studied yellow fever since 1881 and had come to regard the *Stegomia fasciata* as the responsible agent. In screened buildings, Reed had nonimmunes sleep for two weeks in bedding and clothing used by yellow fever patients without development of a single case, when he had some of them bitten by the Stegomia, and within forty-eight to seventy-two hours yellow fever occurred in such victims. Drs. Lazear and Walter Reed lost their lives in establishing the truth of this theory. Their sacrifice, with the subsequent employment of the knowledge by General Gorgas, meant the obliteration of yellow fever, made possible the building of the Panama Canal and permitted the establishment of health resorts in places that previously were but pest-stations. Great tracts which were formally almost uninhabitable, from the ravages of malaria, now afford comfortable homes for a large population and permit the conduct of great enterprizes which were previously thought impossible.

Great as were the benefits secured to the race through the methods employed to control tropical diseases, they were nothing in comparison with the security and sense of safety obtained by the researches into the causes and methods of diphtheria and typhoid fever. The treatment of these diseases occupied a good part of the attention of

the general practitioner in the years between 1875 and 1900. The writer was soon impressed with the futility of the treatment of diphtheritic croup with calomel and tartar emetic, the recognized agents. He saw these cases struggling for breath until a good part of the lung structure would collapse. He continually urged early tracheotomy, but was only able to secure its consideration when it was evident that nothing else would avail. He did the operation 10 times before he was rewarded with a recovery. He was the first physician in Philadelphia to practise intubation, and in 1888, gave an analysis of 25 patients on whom he had practised the latter operation; 22 of these were seen in consultation, in many of whom no measure was longer of any avail. The cases in his own practice all recovered. One patient had to wear a tube twenty-one days before it could be discarded. Of the 25 patients, 13, or 52 per cent, recovered. The discovery of the Klebs-Löffler bacillus as the organism causing diphtheria and the development of serum-therapy have made diphtheria a disease, death from which is inexcusable, as injections of antitoxin given the first day of the disease are invariably effective.

The New York Board of Health met December 15, 1894, and agreed to provide its physicians with antitoxin for the treatment of diphtheria. It was the first city organization to institute such measures. E. H. Place says that the lives saved by diphtheria antitoxin since 1895 may be numbered in millions, yet 15,000 die annually in this country from failure to receive antitoxin at all or to get it sufficiently early. The employment of the Schick-test and the employment of the toxin-antitoxin injections in the positive cases ensures immunity for those thus treated for a period of three and a half years.

Typhoid fever presents another notable example of medical progress. During the Centennial year, 1876, the deaths from typhoid fever in Philadelphia numbered 761, which for the population of the city at that time was more than 100 per 100,000 while in 1923 the mortality from typhoid fever was but 1.55 per 100,000. The deaths given for 1876 were but a part of the record, for sick and infected visitors returned from the Exposition to nearly every hamlet in the eastern half of the United States, many of them to die, causing Philadelphia to lose more in reputation through this disease than she gained by the Centennial Exposition. Purer water, cleaner streets and better drainage have done much to lessen the mortality.

Director Krusen informs me that the record of mortality from this disease in Philadelphia in 1923 is better than that of any large city in this country. The possibility of the control of typhoid fever is better shown by consulting the army records, which present the results of preventive measures that were made obligatory. Chantemesse, in 1896, announced that he had procured a serum from an noculated horse, the inoculation of a guinea-pig with $\frac{1}{5}$ of a drop of which protected it against a dose of toxin fatal to an unprotected animal. Further investigation so demonstrated its efficiency that in the late World War its use was made obligatory. During the Spanish-American war the sickness and casualties from typhoid fever became a national disgrace, as 1 soldier in every 7 had the fever and 1 in 71 died. Among the 4,000,000 serving in the late war there were but 1305 cases of the fever and but 156 deaths. This was equivalent to 1 case occurring in every 3756 and 1 death in every 25,641. Had the incidence and mortality been in proportion to that of the Spanish-American war there would have been 571,428 cases of fever and 56,388 deaths.

Probably no disease has received more consideration during the last fifty years than has tuberculosis. With the discovery of the tubercle bacillus, by Koch, and the introduction of his antitubercular serum it was hoped that the disease might be exterminated. Unfortunately, no serum has effected the expected results, and this disease continues to levy a heavier toll than is exacted by any other. Much has been accomplished by sanitation, in better housing and living conditions, and the recognition of the important part played by the administration of good food and by living in the open. Ransome says that in Great Britain phthisis has steadily declined from 3800 per 100,000 in 1838 to 1305 per 100,000 in 1896. In Philadelphia in 1873, with a population of less than 600,000, there were 2291 deaths from pulmonary tuberculosis. In 1923, with a population of more than 1,800,000, there were 3674 cases reported, with 2162 deaths. With at least three times the population, 100 fewer deaths occurred.

Investigations in later years have changed our views on many obscure conditions. What are called focal infections, originating in abscessed teeth, diseased tonsils, suppurating sinuses, infections of the gall-bladder, appendix, seminal vesicles, prostate or cervix, have been found to have been the source from which originated arthritis, bone affections, chronic inflammation of the ovary and

other lesions. It is quite possible that many persons are unnecessarily mumbling their food, sans teeth, or have sacrificed inoffensive tonsils, but the knowledge that such infections may cause disease through the blood has afforded means to secure improved health, lessen discomfort and prolong life.

One naturally shrinks from the thought of advancing age, with its limitations, its assurance of lessening tenure of life, the possibility of lowered physical and mental vitality; but it has its compensations: It cannot but be a source of gratification that one has known men who have done much to make medicine creditable; men like Atlee, Pancoast, Gross, Agnew, Marion Sims, Emmet and Battey; to have worked with Goodell, Pepper, Tyson, J. M. Da Costa and Osler; to have been associated in medical conventions with men who have elevated and dignified our profession. Among these the name of General W. C. Gorgas projects as a beacon-light. Under his ministrations yellow fever was obliterated from the list of death causes, in Cuba, where it had been continually endemic for one hundred and fifty years. Yellow fever and malaria were banished from the Isthmus of Panama, rendering deaths from all causes there but 8 per 1000, while at the same time our northern cities had a death-rate of 15 per 1000. His work did more to make possible the Panama Canal than the work of any of its engineers. The morbidity and mortality rates would be creditable in the best health resorts. Was it not fortunate that such a man could direct the medical service in the World War? The record already given of the typhoid fever incidence in the army has demonstrated his efficiency. In Great Britian he would have been knighted and placed beyond want for the remainder of his days. When the inevitable time came for his retirement from the active service of the army he was not permitted to rest, but was called on to clean up the pest-places of the world. South America, Egypt and India all demanded his service.

What wonderful privileges are enjoyed by the practitioner of the present day? His is the heritage of the last fifty years of progress, not exceeded by any previous century in the world's history. Tests and reactions are at his command to dispel all doubt. The skeleton, the various organs and their actions can be rendered visible at his command. Pathology, physiology and chemistry, instead of being abstract sciences remote from application, are his handmaidens to make easy his diagnosis and ensure his success in treatment. With

all the opportunities he has gained it becomes a question whether he has not lost quite as much. The increased time he has had to devote to the preparation, for the practice of his profession, in the years when a man is forming the habits and impulses which are to actuate and direct his life; the inability of any one mind to retain all the details necessary for scientific diagnosis and practice and the intense interest of the scientific side of the investigation have necessarily led to specialization. The dependence upon tests and reactions, the greater accuracy of such scientific investigations, have served to exclude the practitioner from the study of the individual, to cause him to lose that psychic inspiration so essential to the encouragement of the depressed physically and mentally ill. One has to guard himself against regarding the patient as the means toward a scientific goal, and lead him to forget that the interests of the individual should ever have first consideration. How often is seen a man, well-qualified for practice, possessed of the requirements for diagnosis and treatment, failing of success, while another much his inferior in intelligence and scientific attainments acquires a large practice because he possesses that human touch, that ability to make his patients feel that their interests only are his first consideration and thus is acceptable to all who come under his influence. The physician today should be unsparing in his acquisition of scientific knowledge, unfailing in his efforts to exercise the most approved tests and reactions, faithfully seek to employ the best treatment, but must never forget that the acquisition of the confidence of his patient is the best drug he can employ. Its acquisition is the goal for which he must constantly strive in order to attain to the highest success.

When the author considers what has been achieved, what is being done and what seems to be gilding the coming dawn, he is constrained to exclaim:

> "Oh! to be alive in such an age,
> When every year's a wonder stage."

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## DISCUSSION

Dr. Charles K. Mills: I feel that I cannot directly discuss the paper of Dr. Montgomery, at least not in its details. I have been relieved from this, however, by the fact that the chairman of the committee, Dr. Beardsley, has made two suggestions in inviting me to open this discussion:

One is that I should limit my time to ten minutes, and I take it that our stern presiding officer, because of his recent remark, will see to it that this injunction is kept. The second suggestion is that I shall restrict my remarks to the influence of neurology, and especially of Philadelphia neurology, on the advance of medicine during the last fifty years. As this second suggestion is in the line of both my sympathy and my sentiments, I shall try to do what I can in this direction. Should some who are present think that my remarks savor of chauvinism, I would say that I do not feel that I will have to apologize for this. Chauvinism, when not of an extreme or offensive kind, is not always deserving of rebuke, whether it be with regard to national or municipal affairs or with regard to a school of thought.

For many years it was the habit, a pleasant one to many of us, to regard the birthplace of American medicine, Philadelphia, as the American medical center, and some of us felt that of this glory we would feign not be shorn. General medicine, as it was then called, or what is now I think not so well called internal medicine, was dominant. Specialism had not then shown its head, but appeared first on the horizon in the early seventies. The specialist, at first, was by no means *persona grata* to the general profession, as some of us cannot fail to remember. It did not come to its own, and then only in part, until a year or two before the founding of the American Neurological Association, in 1874, and the semicentennial of which was commemorated largely in this building last year by a series of meetings and other occasions.

Among the founders of the American Neurological Association were three medical worthies of this city, Dr. Weir Mitchell, Dr. Horatio C. Wood and Dr. Meredith Clymer, and a fourth, Dr. Roberts Bartholow, who afterward became a resident and an important factor in the medical history of Philadelphia. Two of these men afterward became president of this College.

Benjamin Rush, founder of American medicine as he has properly been called, issued the first American work treating of psychiatry and neurology, in 1811. This volume was entitled *Medical Inquiry and Observations of Diseases of the Mind.*

Twenty-seven years later, in 1838, Dr. Isaac Ray published his great volume on the *Jurisprudence of Insanity.* Ray was a New Englander, but spent the last fourteen fruitful years of his life in this city. He was an active member of this College and held the various positions of trust and honor in the city. He became one of the Guardians of the Poor of Philadelphia and in that position was enabled to do much for the insane. He was the first after Rush to give a course of lectures on insanity in this country in the Jefferson Medical College.

After Rush and Ray, medical neurological affairs remained rather stationary for many years until the first systematic work on nervous diseases was published by William A. Hammond, in 1871, who later followed this book by one, in 1883, on insanity.

Dr. Weir Mitchell, in 1872, published his first formal work on nervous diseases, entitled *Injuries to the Nerves and their Consequences,* in the

preparation of which he was assisted by Dr. W. W. Keen, who is fortunately still with us tonight, and Dr. George Moorehouse.

After the volumes of Hammond and Mitchell, articles, treatises, text-books and monographs on neurological and psychiatric subjects appeared in rapid succession. I need only mention here a few of the names of these neurological authors, such as Seguin, Spitzka, Horatio C. Wood, Dercum, Starr, Lloyd, Berkeley, Paton, Spiller, Church and Peterson. Neurological writings were soon so numerous and important in the world of medical letters that neurology became the first among specialties.

One thing in connection with my remarks this evening I wish to particularly emphasize, namely, that to neurological publications general medicine has owed more than can be fully estimated. Before fifty years ago general medical text-books were comparatively few. Looking at some of these, like the text-books of George B. Wood and Austin Flint, and comparing them with recent treatises like those of Osler and Allbutt, the impression made by neurological writing on the pages of these books will at once be recognized. Hundreds of syndromes and diseases have been added to the latter. Great neurological text-books, like those of Gowers and of Oppenheim, now cover more pages that the largest work on general medicine of fifty years ago.

Surgery has been much advanced by neuropsychiatry. I need only refer in this connection to great works like that of Dr. Frazier's *Surgery of the Spine and Spinal Cord* and to a host of other publications on cerebral surgery influenced chiefly by localization.

Many of us who have been interested through long years in Philadelphia neurology feel what I believe to be a justifiable pride in knowing that a Philadelphia school of neurology has come to be recognized both at home and abroad. We feel, also, that we might recall here what has been done both for neurology and general medicine by two Philadelphia institutions, the Orthopedic Hospital and Infirmary for Nervous Diseases and the Neurological Department of the Philadelphia General Hospital.

Dr. James M. Anders: The paper by Dr. Montgomery, it seems to me, contains a wealth of facts of interest to the Fellows of the College. It should prove especially interesting, suggestive and inspiring to the younger Fellows. To project the past into the present, to serve as a guide for the future, is useful. The period covered by the review as presented by Dr. Montgomery constitutes an era of great advance, greater than that of any other previous century, as Dr. Montgomery well states; I think he might have said greater than for all previous time. I want to emphasize in this connection the fact that Dr. Montgomery accomplished an honorable and creditable part of that notable advance in medicine. I would like to say in this connection that those Fellows who can travel back in memory forty-five years into the past with me, will recall that there were not only great surgeons in that day, but great clinicians; men who called themselves general practitioners, not internists, as Dr. Mills has said. They were indeed expert diagnosticians, and their therapeutic judgment was excellent. True it is, they did not advance scientific medicine to any

considerable extent, but we must remember that bacteriology was then a mere infant and very much neglected too by many men who should have accepted its teachings from its birth.

I would like, further, to refer to a case which showed Dr. Montgomery's readiness to cope with unusual surgical conditions forty-five years ago or thereabouts. I requested him to see a young man, aged twenty-five years, who presented all of the symptoms of acute peritonitis following the ingestion of an unusually large meal, including a large amount of sauerkraut. Dr. Montgomery, after an examination, concluded that nothing offered any hope for relief save only operation. He opened the abdomen and verified the diagnosis of peritonitis, which, however, was of the circumscribed, plastic variety. The small intestines were enormously distended and the serous coat lacerated in a longitudinal direction in various places. Without either a moment's hesitation or comment, Dr. Montgomery turned out the intestines, cut through the intestinal wall, along the lines of rupture, unloaded them of their huge contents and then, after first irrigating the abdominal cavity, sutured the intestines very carefully. To my surprise, and I rather think to his own, the patient made an uneventful recovery.

In this place and at this time, it seems to me, mention should also be made of the fact that to Dr. Montgomery belongs the credit of having first suggested the interval operation for appendicitis. This fact is not as generally known as it should be, but it is one that can be, I feel confident, readily substantiated.

# FIFTY YEARS OF SURGERY, 1875–1925*

By JOHN B. DEAVER, M.D.

Man's span of life, according to the Psalmist, "is but as yesterday when it is passed, and as watch in the night." Applied to the life history of surgery during the past fifty years the figure of speech becomes a reality, representing as these years do the dawn after a passing night rapidly developing into the day of brilliant sunshine. Indeed, so rapidly have the science and art of surgery advanced during these years that it is difficult to realize that most of the procedures and the armamentarium at our command today have been developed during the past half-century in our history. What this same period will appear like to him who, fifty years hence, will be reviewing from this same rostrum a half-century or a century of the achievement in surgery it is difficult to foretell. If the ideals of preventive medicine will have been as fruitful as the prophets of today predict, perhaps surgery will have outlived much of its usefulness and will have resumed its original limited field, the treatment of fractures and accidents. And, perhaps, many members of this august body, the College of Physicians, will be looking for or, mayhap, will have already entered upon new fields of activity instead of basking in the sunshine of the past and glorying in the refulgence of their present-day achievement. The rôle of the prophet, however, as you all know is never a pleasant one, particularly in his own country, and I am grateful to your chairman of the Committee on Scientific Business for, and appreciate the honor of, having been assigned the more pleasant and agreeable task of looking backward fifty years.

It is a self-evident fact that the phenomenal advance of surgery during this period began with the epochal discoveries of Long and Morton, and of Pasteur and of Lister. In the eighties ether and chloroform anesthesia had already become well established, but

* Read April 1, 1925.

antiseptic and aseptic surgery were still fighting their way to supremacy. The prejudices of the older surgeon were hard to overcome. He was as loath to discard the methods which had served him with a certain degree of success, as he was to give up his blood-stained, germ-soaked linen duster which had served him for an operating gown. It is not necessary for me to draw a picture of then and now in the operating room, nor of the complete change that has taken place in the entire field of hospital conduct and management. Rather let me proceed to pass in review as best I can some of the outstanding advances in surgical methods.

Fifty years ago (in the words of our own beloved and immortal physician-poet, S. Weir Mitchell), anesthesia, "the highest mercy brought by man to man," had already—

> "Struck from the roll of pangs one awful sum,
> Made pain a dream, and suffering gently dumb"[1]

At that time and for about a decade more general anesthesia, enriched later by the addition of the gas-oxygen method, was almost exclusively used, until its suppremacy was threatened by the introduction of local and spinal anesthesia. This new method has widened the field of surgery and to even a larger extent has reduced the risks of general anesthesia and has transferred many types of cases from the inoperable to the operable class. Still in the process of development, it offers a splendid field for research and profitable investigation; but it is doubtful whether it will ever entirely supplant general anesthesia, although combined with a light general narcosis its usefulness stands unquestioned. The first step in the introduction of local anesthesia is represented by the introduction of the local application of cocaine. The pioneer in filling what proved to be a long-felt want is Karl Koller, who, in 1884, published the first account of the use of cocaine as a local anesthetic in operations on the eye. That the method filled a long-felt want is evidenced by its remarkably rapid spread and development and its adoption in practically every field of surgery. To the late lamented W. S. Halsted belongs the credit of having been the first to use cocaine in general surgery.

The early enthusiasm, however, was somewhat dampened by the toxic effects of the drug, mainly due to imperfect methods of

[1] The Birth and Death of Pain: A poem read October 16, 1896, at the commemoration of the fiftieth anniversary of the first public demonstration of surgical anesthesia. By S. Weir Mitchell, M.D.

manufacture and its consequent admixture with impurities, as well as to the limited facilities for its production, so that the demand being far in excess of the supply caused an enormous inflation in its price. But the synthetic production of the drug soon corrected both these evils, and at the same time led to the discovery of many synergetic drugs. Notable among the latter is novocaine, discovered in 1905 by Adolph Einhorn, which seems to combine all the requirements of a local anesthetic without any of its disadvantages.

Thus armed with the means of making "suffering gently dumb" and enriched with the growing power of controlling infection, the surgeon boldly threw down the barriers that had hitherto blocked his path, especially in the domain of abdominal surgery. But in spite of Lister's antiseptic methods, the early days of this new era witnessed many discouraging results, and thoughtful men soon realized that Lister's theory of air-borne infection was only partially complete, especially when applied to intraperitoneal operations. Prominent among such keen observers stands Lawson Tait, who was among the first to emphasize asepsis rather than reliance on chemical antisepsis. Animal experimentation, also, helped to demonstrate the destructive action of certain chemical antiseptics on certain tissues, especially within the abdominal cavity. And at this time Pasteur himself boldly attacked the theories of some of the eminent physicians of his day on the cause of puerperal infection by showing that the infection was carried from a sick woman to a healthy one by the doctor himself, and illustrated his theory by drawing on the blackboard the picture of the culprit—the now familiar streptococcus in chains. This may be said to be the actual beginning of the revolution in operative technic consisting of strict surgical asepsis of all instruments, the use of rubber gloves, sterilized operating gowns and scrupulous asepsis applied to everything and everyone connected with the operation. Today these measures are so much a matter of course that it seems almost banal to mention them.

Hospital construction naturally kept pace with these advanced ideas and there is the same difference between the modern hospital and the hospital of half a century ago as there is in the surgery of then and now.

I have already mentioned that the earliest field invaded by the newer surgery was the abdomen. Abdominal surgery, which before 1875 was considered more or less criminal surgery, rapidly came into its own and exploratory laparotomy was from now on considered a

perfectly legitimate procedure. Indeed, the abdomen henceforth (to use the apt expression of our great and greatly beloved Keen) was destined to become the playground of the surgeon. While many of the "ectomies" now in general use had already been attempted in the early days immediately following the introduction of ether anesthesia, they were abandoned as unsuccessful and dangerous. These were now being revived under the beneficent sway of asepsis, improved technic and increased familiarity with the procedures. Not only that, but entirely new operations were being devised, many of which represent some of the most striking contributions of our era to the history of surgery.

The decade from 1875 to 1885 witnessed such important innovations as Porro's Cesarean section with excision of the adnexæ; Freud's excision of the uterus; Lawson Tait's operation for extra-uterine pregnancy. Billroth, in 1880, performed the first pylorectomy for cancer of the stomach. This was followed by a rapid succession of anastomotic operations, the first and most familiar of which is Wölffler's gastroenterostomy, in 1884. The gall-bladder was successfully removed by Langenbuch in 1882. Each of these procedures, modified and improved, has become a daily occurrence in all large clinics.

The year 1886 is marked by Fitz's memorable study of the pathogenesis of appendicitis, which perhaps more than any other single investigation has changed the concept of the causes of intra-abdominal infection and eliminated the then-prevalent term of idiopathic peritonitis from our medical vocabulary. During the next few years surgery was enriched by O'Dwyer's improved method of laryngeal intubation, a distinctly life-saving measure, but the indication for it is being reduced to a minimum by the present-day methods of antitoxin treatment of diphtheria. Mutilating bone-surgery and amputations were being replaced by nonmutilating orthopedic and plastic operations. MacEwen's osteotomy, opening large joints, restoring ankylosed limbs, belongs to the period before the close of the nineteenth century. All these are matters of daily occurrence and enjoy a large degree of certainty of good results. Horsley's laminectomy, also, belongs to these years, and at this time suture of the heart was attempted with success. Gynecology was enriched by Wertheim's operation, and so the story could proceed from one innovation to another and from one advance to another.

During this period of evolution it was but natural that the instrumental armamentarium of the surgeon should keep pace with advances in surgery. The number of new devices is legion, but it may be well to mention some of the more outstanding ones which have facilitated our work. Hemostats were modified and improved; the Kocher forceps is a notable contribution; the ingenious Murphy button still serves a useful purpose for anastomotic operations, although most surgeons today have returned to suturing as a more desirable method of joining resected viscera; a notable innovation is also represented by the Paquelin cautery. Posture during operation came in for adequate consideration, and we use the Sims' position, the Trendelenburg position and the like, on tables expressly fashioned for such changes in position. Practically every surgeon has devised some modification of the usual instruments to facilitate his work.

It was but natural that the entire change in surgical methods, and I may say surgical thinking, should demand increased facilities for diagnosis. The development of endoscopy at this time supplied this desideratum and placed at our disposal the ophthalmoscope, the esophagoscope, the bronchoscope, the rectoscope, the cystoscope, etc., by which direct inspection of pathologic processes has been greatly facilitated. Whether these devices gave the impetus for the rise of the surgical specialties, or whether the rise of the specialists produced the instruments, the fact remains that the years between 1890 and 1900 saw the separation of surgery into specialties which today is taken entirely for granted, such as the treatment of diseases of the eye, ear, nose and throat, genitourinary surgery, and so on.

The surgeon of fifty years ago might have been able to predict some of the advances in surgery which I have attempted to record, but it is doubtful whether anyone, no matter how imaginative he may have been or how optimistic, ever dreamed of the possibility of direct inspection of practically all parts of the human body as provided for us by that most notable and I may say romantic invention of the physicist, Wilhelm Conrad Roentgen. Does it not sound like a page from a romance that the accidental placing of a glowing electric-light bulb upon a book containing a metal key, and under which lay a photographic plate, should have led to the discovery of a ray of light, invisible to the eye, capable of traversing solid substances? From now on the demonstration of pathologic

changes, of injuries to the bony system become possible. Not only that, but with the development of the roentgen-ray today we are able to inspect the body viscera and observe function, so that roentgen-ray diagnosis has become an almost indispensable diagnostic adjunct, particularly in disease of the lungs, the heart, the gastrointestinal and the genito-urinary tract. However, I have on more than one occasion registered my protest against allowing roentgen-ray diagnosis to replace rather than to confirm or enhance clinical diagnosis. The danger is an ever-present one and the warning bears repetition.

During these years, then, the years of acquisition, if I may so call them, we were learning much about how to operate, and at the same time why to operate and when to operate. In other words, surgical pathology rapidly found a most important place in surgical endeavor. Hitherto pathology had been limited practically to external pathology, and the dead in the postmortem chamber were teaching the living. But henceforth it was destined to be superseded by internal pathology, whereby the living teach the living. Pathology of the living is the term for this so happily coined by that master surgeon, Sir Berkeley Moynihan. This unquestionably represents the most vital factor in medicosurgical advance. Animal experimentation, of course, has played an important rôle in progressive work; indeed, it represents a large part of the pathology of the living, and through it there have been opened up entirely new paths of investigations for the physiologist, the surgeon and the pathologist, such as glandular function, neuropathology and localization, functional pathology of the gastrointestinal tract, etc.

The phenomenal development of bacteriology during these years provided another notable contribution to our knowledge of both why and when to operate. New discoveries in this sister science succeeded each other with bewildering rapidity and were gradually routing from their lairs the hidden causes of many infections. To mention only a few, I may call attention to the discovery of the bacilli of anthrax, of gas gangrene, of diphtheria, of meningitis, the gonococcus, the pneumococcus, streptococcus, staphylococcus, the colon bacillus. These naturally led to the discovery of other germs related to visceral lesions which concern the medical man and the surgeon alike in their various fields of activity.

Closely allied to this new avenue of research is the science of serology, which has written an entirely new chapter in the history

of our profession. It has revealed the importance of the organs of internal secretion and has thrown light on many obscure and delicate biologic reactions. Its demonstrations of the influence of glandular activity on metabolism and vital functions, on growth and regeneration are among the most noteworthy contributions to the medical sciences. Surgically, its import lies in the revelation of the interdependence of all the components of the endocrine system which has brought about so marked a change in our conception of certain disease processes and a resulting change in therapeusis.

In line with this is the recrudescence of blood transfusion. The idea of blood transfusion was germinating in the minds of surgeons for many centuries. Indeed, it was attempted as early as 1667 by a Frenchman, Denis, but with such results that any further use of the procedure is said to have been prohibited by parliamentary edict. It was repeated from time to time by other surgeons with indifferent or altogether unfavorable results. No wonder, since for its success was needed, not only the strict antisepsis of modern times, but also the advances in vascular surgery of our era. Provided with these and with a thoroughly physiologic habit of thought, it remained for our own Crile, about thirty years ago, to reintroduce the procedure which in its subsequent development has become one of the most useful measures at the disposal of the surgeon in great emergencies. The correlated method of storing up collected blood with the addition of sodium citrate has added much to the value of the procedure.

The why to operate is but the application to practice of a new manner of thinking which was developing during these years. It can be best expressed as the pathologico-physiologic habit of thought. This new habit of thinking is no doubt responsible for the return of surgery to the dignified profession of today. Where formerly the surgeon was merely the handy-man for the internist, today the internist is, or should be, glad to have the surgeon not merely as his operator but as his coöperator. Surgery and medicine are now too closely allied ever again to be so widely separated as in former days. It is to the interest of the patient, the final goal in all our work, that this entente become closer and closer in order to insure the best results. I shall revert to this later on. The surgeon's knowledge of when to operate should be called into action early and it should be left to him and not to the internist to decide. Every surgical disease has "its surgical hour" which, taken at its best, bids fair to lead to victory.

If, as I have intimated, the new science of bacteriology received a marked impetus through the new habit of surgical thinking, surgery in turn owes it a vast debt in one of its most triumphant fields of usefulness, and that is the recognition of the surgical hour that bids fair to lead to victory. We need no figures to convince us that the timely recognition of, and timely intervention in acute disease of the abdomen is one of the outstanding achievements of modern surgery. There is no way of reckoning the countless numbers that have been saved by this advance. And for many chronic infections there is the possibility of a cure by removal of the infected organ, such as the appendix, the gall-bladder, chronic pus tubes, cystic ovaries, the infected uterus, the diseased kidney, the enlarged prostate, the spleen.

It may be consoling, to the laymen particularly, that there still are some organs that have escaped the scientific greed of the surgeon, to use the term of a French surgeon. Among these are the pineal gland and the suprarenal capsule, the pancreas, as a whole, the medulla oblongata and the cardiac valves.

But even the heart and the lungs are nowadays not closed to the path of the surgeon's knife. In some quarters surgery claims to have cured certain types of cavernous pulmonary tuberculosis and bronchiectasis. Operative interference in pulmonary abscesses has become much safer than ever before. Surgery of the heart, it is true, is being written about probably more than it is being practised; but the results are encouraging, considering that this is the early stage of development of a very delicate procedure.

Brain and spinal cord surgery have made remarkable strides during the past twenty-five years, particularly in the localization diagnosis of disease of these regions, and this advance is one of the best illustrations of the coöperative work of the clinician and the surgeon. Although the special structure and physiology of the brain and its centers interfere with the absolute success of surgery in this region, nevertheless there can be recorded a distinct gain in the treatment of tumors of the cortex and even of deep-seated ones in the cerebellopontine angle and the hypophysis, which together with the surgery of the spinal cord excite the well-deserved admiration of the profession. Rapid strides in vascular surgery mark an outstanding achievement of our time, especially in the treatment of traumatic aneurysms.

In a retrospect of more recent years war surgery supplies an

important chapter. It is interesting to note that the emergencies aroused at the time witnessed a return to the early methods of chemical antisepsis as represented by the much-lauded Dakin's solution. Débridement of wounds, although practised many years ago and much in vogue even before the war, was revived. Plastic surgery received a tremendous impetus during these years, the effects of which are perhaps more noticeable in civil surgery than any other procedure stimulated by the exigencies of war.

It must remain for the younger generation to evaluate what the war brought forth in surgical methods, and I shall leave this aspect of my subject to them.

Our history, as I have endeavored to point out, shows an ever-increasing tendency toward a consideration of why and when to operate, a practice that was scarcely possible before this era. Formerly the main reason for operation was the immediate saving of life, without a great deal of thought of the resulting possible morbidity. Today we are in a position to aim at conserving life with a very high degree of restoration of function. The essential desiderata for attaining this ideal and for which the coöperation of all branches of the medical sciences must be brought into play are adequate diagnosis, and to no less extent adequate preoperative and postoperative treatment. These are but part of the physiologic habit of thought which marks our time, but they demand the free and willing coöperation of the clinician, the surgeon and the scientist.

We can point with pride to the problems that have been solved, but we dare not fail to realize that there are still many that seem to baffle solution. I need but mention our ignorance of the cause of cancer which makes our treatment of that malignant disease still a matter of empiricism, and which of itself is enough to humble the proudest among us.

Medicine and surgery owe a vast debt to nonmedical men—Pasteur a chemist, and Roentgen a physicist. Perhaps the solution of this problem will also come from one of our sister sciences.

# COCCIDIOIDAL GRANULOMA*

By DAVID RIESMAN, M.D.

AND

FLORENCE E. AHLFELDT, M.D.

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Synonyms. Coccidioidal granuloma; Coccidioides immitis; Oidiomycosis; Oidioidal granuloma.

Coccidioidal granuloma is a rare disease which made its first appearance in literature in 1892 in a report by Wernicke, of Buenos Aires. The second case, the first in this country, was recorded, in 1896, by Gilchrist and Rixford, who studied the parasite and called it Coccidioides immitis. In 1900 Ophüls gave an excellent account of the cultural characteristics of the organism. P. K. Brown, in 1907, collected 18 cases of the infection, adding 2 of his own to the list. Dickson, in 1915, reviewed the literature; Bowman, in 1919, studied the *x*-ray findings; Taylor, in 1923, and Hammick and Lacey, in 1924, reported several instances of the disease.

It is a striking fact that the majority of the cases have occurred in California or in persons who had lived in California, particularly in the San Joaquin valley. Our own case was that of a boy who had spent a summer in New Mexico.

The disease affects chiefly the male sex. Of 82 cases collected by us, only 4 were in the female sex. Race appears to play no part. As for occupation, we find that 19 patients were farm laborers, 5 cattlemen and 5 railroad workers. Single cases have occurred in nearly all trades and professions; 1 patient was a physician and 1 was a student. With respect to age, we find that of 76 cases, in 41, or over one-half, the age was between twenty and forty years, and in 8 under ten years.

Our own patient was a little boy, aged five years. He was brought to the office of one of us (Dr. R.) on January 11, 1924, because of persistent low

* Read April 1, 1925.

fever. His parentage was good except that a number of the family had asthma and hayfever. He himself had been well until he had intestinal influenza in March, 1923, which left him with a fever and a cough, lasting until September of that year. He then had an attack of pneumonia, from which he made a prompt recovery. It was, however, followed by otitis media, necessitating puncture of both drums. Thereafter, the temperature dropped to normal and remained so until November, 1923. Since his attack of fever, in March, it was noticed that he had some enlargement of the posterior cervical lymph nodes and a lump in the right axilla.

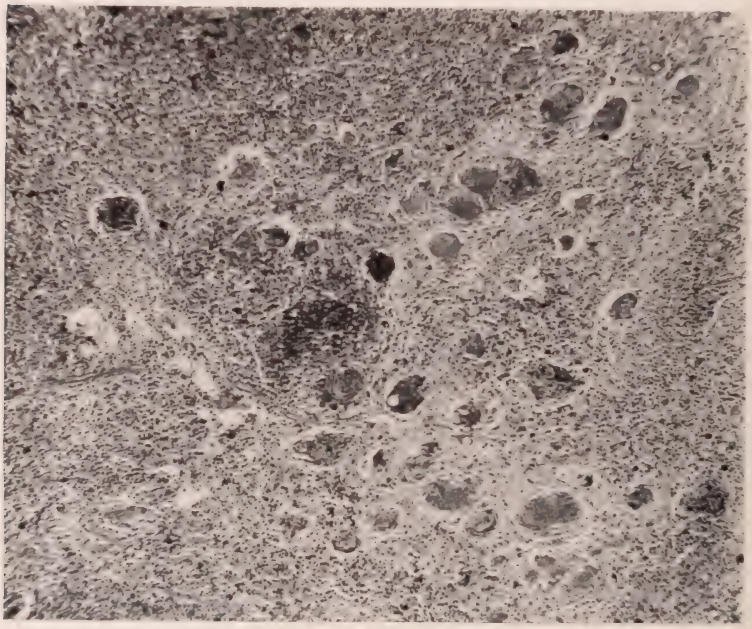

Fig. 1.—Low power, showing granulation tissue with giant cells and organisms.

In November, 1923, he had another bronchial cold with fever lasting about two weeks. The tonsils and adenoids were then removed; but, contrary to expectations, another febrile cold set in just before Christmas and persisted up to the time when the boy came under our observation. The temperature, it was stated, was usually normal in the morning, rising to 101° F. by 6 P.M. The cough, which in the early attacks had been somewhat asthmatic, was now less severe.

On physical examination a mass of large glands was found on the left side of the neck just above the inner end of the clavicle, while smaller nodes extended upward to the hair-line posteriorly. One large node was found

on the right side near the angle of the lower jaw. The axillary glands were just palpable. A blood count made at that time gave the following results: White blood cells, 22,800; red blood cells, 4,650,000; hemoglobin, 70 per cent; polymorphonuclears, 70; lymphocytes, 7; large mononuclears, 6; transitionals, 3; eosinophiles, 12; basophiles, 2.

Our first suspicion was that the glands were tuberculous—a von Pirquet test had been positive—but the distribution, especially the involvement of the suboccipital nodes, was anomalous. A gland was therefore excised by Dr. E. L. Eliason and studied by Dr. Herbert Fox, whose report was that he found evidence of coccidioidal granuloma. Through an oversight the excised gland had been thrown into fixative solution, so that cultures

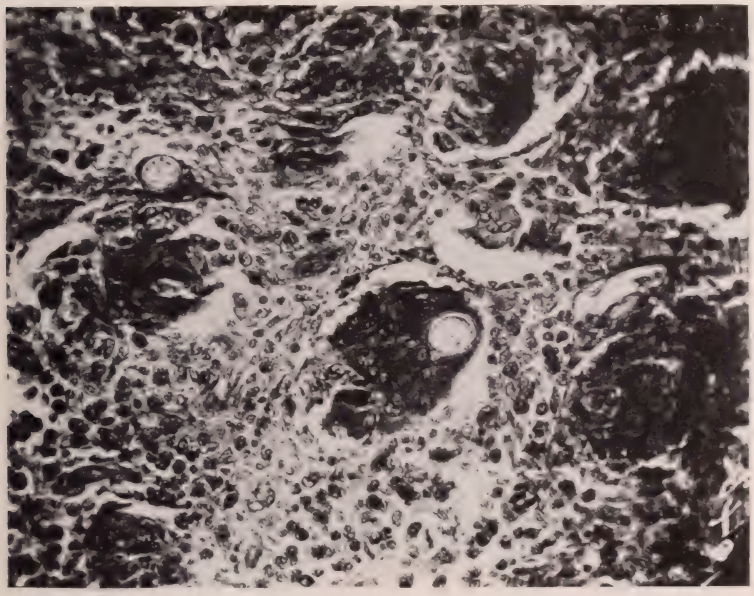

Fig. 2.—High power, showing giant cells with organisms.

could not be made from it, but cultures were made subsequently from the pus of broken-down glands and showed the characteristic organism and confirmed the diagnosis.

The temperature became more and more hectic, the cough hard and brassy. The glands increased in size and new ones developed. Dulness could be detected over the left upper chest. Two fluctuating swellings appeared on the scalp and in the pus obtained from them the coccidioidal organism was demonstrated. Another swelling, gradually increasing to large size, appeared over the right chest posteriorly; in addition, the right pleural cavity became the seat of an effusion that required tapping. But only for a day or two was the child comfortable after the tapping, for the fluid

quickly returned. The abscesses in the scalp continued to drain a grayish purulent fluid mixed with a little blood. Much distress was caused by abdominal distention, which we attributed largely to deep-seated glandular masses and ascites.

An *x*-ray examination of chest by Dr. Pancoast showed extensive masses in the mediastinum.

The boy, who was sensible and patient beyond his years, grew steadily weaker in spite of various methods of treatment, including arsenicals, iodides and Alpine light given by Dr. Percival Nicholson, and died May 2, 1924, about eight months after the onset of definite symptoms. There was no autopsy.

Fig. 3.—High power, showing sporulating form.

Biology, Nomenclature and Classification of the Organism. In regard to the biological position of the organism there is room for much discussion. It is not a protozoön, but a mould. Some have placed the genus Coccidioides in the class of Ascomycetes. As yet no final classification has been made. According to Ophüls there are three diseases which resemble each other somewhat: that which occurred in San Joaquin valley, called coccidioidal granuloma; that found near Chicago, called blastomycosis; and that reported from Missouri, called sporotrichosis.

Biology of the Organism. The organism is a fungus which grows in the tissues in the form of spherical, double-encapsulated bodies of from 20 to 40 microns in diameter and often filled with spores. Budding has not been observed within the tissues. On culture media, especially glucose agar, it grows as a delicate, white, fluffy disk from which project the slender hyphæ which are never developed within the body. Whether or not the organism produces a soluble toxin is not known.

The fungus is pathogenic for rabbits and guinea-pigs. In our experiments the guinea-pigs died in from twenty to thirty days after a great loss in weight, often up to 50 per cent. At autopsy, characteristic nodules were found in the lungs and liver. It is also worth noting that, in our experiments on animals, the testicles become involved irrespective of the point of inoculation.

The suggestion has been made that the kangaroo rat may play a part in the spread of the disease. It was observed that our boy drank water from a well in which a kangaroo rat was found, the dead rodent being covered with a whitish mould. Other persons drank from the same well but did not develop any disease. Through the kindness of Dr. Herbert Fox we have secured two kangaroo rats and are investigating this point.

No light has as yet been thrown upon the question as to why the disease prevails much more in California than elsewhere. It may be that the organism finds in that section certain conditions favorable to growth, either in the sense of an intermediate host or because of something else as yet unknown. No doubt the fact that the disease has been better studied in California contributes to its greater frequency of discovery.

Pathology and Pathogenesis. In the majority of cases the atrium of infection seems to be the respiratory tract, since the disease begins as a rule with a cough and signs in the lungs and with early involvement of the regional lymph glands.

A few instances of gastrointestinal invasion are recorded, the symptoms in this group leading to a diagnosis of typhoid fever.

Involvement of the joints and of the skin without visceral or respiratory infection has been observed.

Lesions in the lung resemble those of tuberculosis. There is a widespread occurrence of pinpoint nodules. These nodules may be found anywhere. The tissue between the tubercles is generally congested and edematous. Giant cells are seen, and either within

or near the giant cells are the organisms. The affected lymph glands in our case, as well as in others recorded, showed chronic inflammatory changes resembling tuberculosis in the sense that there were areas of granulation tissue with many giant cells. The characteristic structures of the organism were seen in and near the giant cells. In one slide we found internal sporulation, but nowhere any budding or growth into mycelia.

In the average human case the end-symptoms suggest tuberculosis of the lungs or tuberculous adenitis, but the discovery of the organism in the sputum or in the discharge from the glands will lead to a correct diagnosis.

There are, however, two points of significance that were observed in our own case: (1) The peculiar location of the enlarged glands in the occipital region, in the axilla, etc., and (2) the extremely rapid breaking-down of the glands when once the breaking-down process had started. Furthermore, the discharge was more abundant and different in color (*café au lait*) and in consistency from tuberculous pus.

Differential Diagnosis. We have already adverted to tuberculosis and need say no more about it. In cases in which glandular involvement predominates all the various lymphatic diseases have to be borne in mind. Leukemia, Hodgkin's disease, glandular fever (infectious mononucleosis), lymphosarcoma, etc. Of greater importance in the differential diagnosis is the disease called *blastomycosis*.

In this affection the skin lesions are generally primary, remain chronic, and are considerably improved by large doses of potassium iodide. The disease may, however, become generalized, and there are several instances reported in which the meninges were involved.

Just as coccidioidal disease is most common in California, so blastomycosis occurs most frequently in and about Chicago. It is probable that a greater interest in the disease accounts for this.

Blastomycosis is carried apparently only by the bloodstream, while coccidioidal granuloma may spread both by the blood and by the lymph channels. In blastomycosis budding is seen both in cultures and in the smears from the affected tissue.

*Actinomycosis*. This disease is caused by the *Actinomyces*, or ray-fungus, and is characterized by tumor-like masses of inflammatory tissue which affect especially the jaw or tongue. These masses soften and discharge a puriform liquid containing small granules

of a sulphur-yellow color, made up of the fungus. Metastasis to the internal organs is sometimes observed and when it occurs the blood rather than the lymph seems to be the medium by which the disease is spread. The history of the occupation, location of the lesion and the finding of the organism leads to the diagnosis of actinomycosis.

*Aspergillosis.* This disease, caused by genus aspergillus, has been reported, especially from France. Many of the cases have been in those who have had to do with the care of pigeons. In man it attacks chiefly the lungs, producing lesions and symptoms similar to tuberculosis from which it is to be distinguished only by finding the mycelial threads and spores of the fungus in the sputum.

*Sporotrichosis.* This is caused by fungus *Sporotrichium*, a sporothrix. The disease generally takes its origin at some point of slight injury. At the same time or later a subcutaneous nodule may be felt which gradually enlarges peripherally. It softens, discharging a seropurulent fluid. Lymph channels may be felt as a hard cord. The disease responds to potassium iodide.

Coccidioidal granuloma, blastomycosis, as well as the other fungoid diseases, should be thought of:

1. If the sputum in a case of chronic pulmonary disease does not show tubercle bacilli on repeated examinations.

2. If the patient has lived on the Pacific slope. In all pulmonary cases not typically or definitely tuberculous the sputum should be cultured on various media, especially glucose agar, for other organisms than the tubercle bacilli, for the coccidioides, the streptothrix and other fungi and yeasts.

Whenever the lymph nodes are enlarged in atypical cases, a gland should be removed for biopsy; part of it should be used for culture and part fixed for staining.

With the free intercourse that obtains in this country among the citizens of all the states it is improbable that blastomycosis is limited to the environs of Chicago and coccidioidal granuloma to the Joaquin valley of California.

Prognosis. If the coccidioides infection has become systemic, it is grave. Only in those cases in which it was localized and the part amputated, has the patient survived.

Treatment. Unfortunately, as far as we know, there is nothing which has any effect. Surgery is the only remedy in cases of superficial localization.

Acknowledgements are to Mr. H. S. Colton, for his liberal support, and to Dr. Herbert Fox, Dr. Allen J. Smith and Dr. F. Weidman for many courtesies.

## DISCUSSION

Dr. Eugene L. Opie: This case of Dr. Riesman's is one of the few instances of systemic coccidioidal granuloma recognized during life. I was a student of Dr. Gilchrist at the time when he described the second recorded case of this disease, and he showed us sections of the remarkable lesion containing the encapsulated spore-containing microörganism. He regarded it as a protozoan parasite belonging to the sporozoa and resembling coccidia. A few years later, Ophüls succeeded in growing the organism and demonstrated that it had the characters of a mould. He called it Oïdium coccidioides. Dr. Riesman has spoken of the confusion in regard to classification of this organism. It belongs to the hyphomycetes or the Fungi imperfecti, which include almost all the pathogenic fungi. Some have associated it very closely with the parasite of blastomycosis, a disease of which Gilchrist described the first instance. Ricketts made a very careful study of the fungi found in association with blastomycosis and coccidioidal granuloma, and, though he believed that a variety of species were concerned, placed all of them in the same group. He designated them oïdia. It is not difficult to understand why there has been so much confusion concerning the classification of pathogenic fungi. They have been classified in accordance with their morphology. The blastomyces, saccharomyces or yeasts are round budding organisms, and the oïdia are thread-like in structure. The character of spores has been an important basis of classification, and fermentation of sugars has served to separate different types. Jörgenson, an authority upon fermentation, found that yeasts which usually multiply by budding may under certain conditions form endospores. Hanson, another student of the same subject, found that certain species of Saccharomyces cereviciæ, which are usually round, may form threads or mycelium at high temperature. With these variations among well-known types, classification of pathogenic forms becomes exceedingly difficult. The organism of coccidioidal granuloma has been regarded as distinct from that of blastomycosis, because it forms endospores in the tissues and, at times, in cultures.

# SPONTANEOUS RUPTURE OF THE HEART*

## A Clinicopathologic Study Based on 22 Unpublished Cases and 632 from the Literature.†

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and

C. CROWELL, A.B., B.S.

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Spontaneous rupture of the heart is of sufficient rarity to occur but seldom in the experience of a single individual; its dramatic qualities are such, however, that the individual frequently wishes to record his experience, with the result that medical literature contains a comparatively large number of single cases or small group reports. This, together with the coincidence of several cases within a short period at the Philadelphia General Hospital has led us not only to present in detail 22 hitherto unpublished cases that could be collected from this and other hospitals of Philadelphia, but also to tabulate the important items of 632 cases from the medical literature of the past fifty years. The incidence of only 7 cases in 16,000 autopsies at the Philadelphia General Hospital is similar to that reported by Romeik at Munich (7 in 13,000 autopsies), but less than the Leipzic series (9 in 8000 autopsies).

The beginning of our search was made with the year 1872. Except for a few cases of historical interest, it was felt that cases prior to 1872 would not have been studied in a sufficiently modern way to fit in with the analysis of the later cases. In 1872 Quain published his important article "On Fatty Diseases of the Heart," which not only presented data on a large series of hearts that had

* Read May 6, 1925.

† We take this opportunity of expressing our thanks to Drs. A. J. Smith, J. Eiman and J. R. Paul for the material they have offered us, and especially to Dr. S. B. Wolbach for the series of 9 unreported cases from the Peter Bent Brigham Hospital.

ruptured, but also announced principles that dominated the thought on this subject for many years. In fact some of his statements, misleading rather than incorrect, and hardly possible to have been improved upon in the state of cardiac pathology of that day, are responsible for some of the mistaken views that are held on the subject of cardiac rupture today. Quain was correct in asserting that "Rupture of the heart may be said never to occur spontaneously when the heart is healthy." Accurate on the whole is his description of the appearance of the tear, its relative frequency in the various chanbers and in the two sexes, the importance of old age and of most of the symptoms observed. His description of the pathogenesis and the myocardial lesions, however, was very unsatisfactory. Twenty-seven per cent were considered to be due to fatty degeneration and 6 per cent to softening. Ulceration, interstitial hemorrhage, abscess and bursting of an aneurysm were also mentioned, while the coronaries were barely noticed. In modern text-books of pathology such statements occur as "The most frequent causes are fatty degeneration of the muscle and occlusion of the coronary arteries; less commonly, myomalacia, abscess, gumma echinococcus cysts and new growths are responsible." One of the best pathological text-books states that spontaneous rupture usually occurs with chronic aneurysma cordis, necrosis following coronary disease, marked fatty infiltration, especially if combined with fatty degeneration or brown atrophy; the latter an obvious "left over" from the days in which the condition of the coronary arteries was seldom reported upon and their significant relation to myocardial lesions apparently not well understood. In the present analysis particular attention is paid to this point, which has also been emphasized by Robin and Nicolle.

Methods. During the past fifty-two years there have been valuable summaries of this subject by Minet and Le Clerc, based on a study of 77 cases; by Robin and Nicolle, based on 177 cases; Quain's 100 cases previously mentioned. These together with the 22 cases of our own series and the 278 cases analyzed by us from the literature make a group of 654 cases on which this study has been based. Valuable summaries by Elleaume and Barth had to be omitted from our figures, as it was probable that some or many of their cases had been used by Robin and Nicolle. As the latter's cases were tabulated as individuals, we were able to compare them with our lists and thus eliminate 26 duplicates. As Quain's list may also contain

some duplicates, though probably few, we have preserved the identity of the main sources in our tables. Thus the reader may select as he chooses, as well as compare the various sources. The 278 cases that we have abstracted from the general literature were secured from 191 references in the *Index Medicus* and the *Index Catalogue* of the Surgeon-General's library.* In each case, as far as possible, information was tabulated about the sex, age, occupation, habits and past history, clinical diagnosis, onset of duration of severe cardiac symptoms, symptoms attributable to the rupture, duration of life after probable occurrence of rupture, whether or not it happened during sleep, if hemopericardium was present, site, size, nature of tear in the myocardium, whether partial or complete, cause of rupture, contributing lesions, condition of coronaries and miscellaneous remarks. It was, of course, impossible to secure all of this information in the three collected reports above mentioned, and even many of the single reports were deficient—an evidence of the inability of the average medical writer to give complete statements on even the simplest subjects. Obviously, too, the results obtained are much more reliable in some particulars than in others. Thus the evidence on such concrete simple items as age, sex, chamber ruptured and so forth can hardly be incorrect and in such large numbers must represent closely the true picture. Other details where the author's judgment is concerned, however, such as "survival after rupture" and "underlying cause," must be taken with greater reserve.

Before considering the results of the statistical study some details of our own 13 cases, which are fairly representative of various types, will be given.†

Case Reports. Our own series of cases can be divided into the following five categories: (1) Coronary sclerosis and thrombosis with myocardial fibrosis and necrosis, 9 cases; (2) coronary sclerosis and thrombosis with myocardial fibrosis only, 2 cases; (3) coronary sclerosis only with myocardial fibrosis and necrosis, 5 cases; (4) coronary sclerosis only with myocardial fibrosis, 2 cases; (5) no evidence about the condition of the coronaries, 4 cases.

Group I. *Coronary Sclerosis and Thrombosis with Myocardial Fibrosis and Necrosis.* Case I.—W. L., a senile dement, aged seventy-nine years,

* References to these cases are too numerous to be included here, but will be furnished by the authors on request.

† It has not been possible to copy the exact words of the autopsy reports in all cases. The authors, therefore, assume responsibility for the statements made.

was admitted to the Psychopathic Department of the Philadelphia General Hospital, November 7, 1923, on the service of Dr. Rhein. No history of heart disease was obtained, though his feet were edematous, his heart sounds weak and peripheral vessels sclerotic. No murmurs, arrhythmia or cardiac enlargement were found. Urine and blood Wassermann tests were negative and the blood urea was 19 mg. The blood pressure was not taken. His condition continued unchanged until 1.30 A.M. of November 24, when he was found dead in bed, without the patients in the next beds having noticed anything unusual. Thirty minutes earlier he had talked normally with the night nurse.

At autopsy (P. G. H., 8236) I found the pericardial sac bulging with fluid and clotted blood (totaling over 350 cc.), which was found to be due to a small jagged opening, about 6 mm. long, in the posterior surface of the left ventricle, and slightly nearer the apex than the base. This did not at first admit a probe without danger of causing an artefact, but after the heart was opened it was found to connect diagonally with a similar opening in the endocardium near the posterior papillary muscle of the mitral valve and to admit easily a small probe. At neither point was there any clot. The heart weighed 400 gm. and measured 12 by 9 by 7 cm. It showed a thick, fatty, epicardial layer, with prominent and tortuous coronary arteries and mottled myocardium; toward the apex this almost resembled the scar tissue of a healed infarct. The muscle was flabby, but not tough. There were no pericardial adhesions. The right ventricle was apparently normal, its wall averaged 4 mm. in thickness and it contained a small amount of mixed red and white clot. The mural endocardium of the left ventricle was especially thickened at the lower end of the septum, and the myocardial wall was thinner at this point (6 to 8 mm.). The myocardium elsewhere measured from 10 to 14 mm. in thickness and showed no noteworthy fibrosis except in the area mentioned. The tips of the papillary muscles and chordæ tendineæ were very slightly thickened. The mitral and aortic valves were slightly thickened. The valve orifices measured: Mitral, 10; aortic, $7\frac{1}{2}$; tricuspid, 10; pulmonary, 7 cm. The orifices of the coronary arteries were somewhat sclerosed, especially the left. The right coronary artery, about 2 cm. from the orifice, was occluded with a dark red adherent clot, extending into the two branches for several centimeters.

*Anatomical Diagnosis.* Hemopericardium. Acute infarct of myocardium with rupture following coronary thrombosis. Myocardial degeneration with cardiectasis due to coronary sclerosis.

Other items of interest in the autopsy were a markedly atheromatous and fragile aorta, a phlebolith in the splenic vein, chronic splenitis and mixed nephritis, cerebral arteriosclerosis, thrombotic softening and convolutional atrophy.

*Histology.* Heart: Left ventricle: The subpericardial fibers are best preserved, though even here they are cloudy and swollen with indefinite striæ. There is some fragmentation and pigmentation, the nuclei are found to be large and rectangular. Deeper, these phenomena are more prominent and interstitial fibrosis appears, with much distortion of muscle fibers, several areas of fibrosis, containing but few muscle remnants, fill

whole low-power fields. Fibrosis is most marked about the vessels. Serial sections through the ruptured area of the ventricle show a complicated picture of muscle degeneration, anemic infarction and, at a distance from the rupture, a separate, partly organized infarct. The jagged, oblique sinuous line of rupture can easily be traced through a definitely necrotic space, in an irregularly flat pyramid with the apex almost at the pericardium. The fibers are traversed in their long axis near the endocardial surface by the rupture, but transversely through a narrow subpericardial band. The path of the rupture is lined by the bare fibers in some places, in others by a smooth composite of necrotic and interstitial tissue and infiltrated cells of various kinds. No thrombi are present. The tissue in which the rupture lies presents in a more marked degree the same lesions as more distant areas, but so close to one another that a continuous line of lessened resistance resulted. At some points, reaching almost to the line of rupture, the muscle is merely swollen and wavy, with more or less loss of striæ and tendency to pyknosis of muscle nuclei. There is considerable perinuclear pigment and some hyaline and fatty degeneration. At other places there has been marked complete loss of muscle fibers, giving a lacework appearance to the interstitial tissue, and this may be with or without cellular infiltration. Many areas have a dirty, slate-blue appearance (with hematoxylin and eosin), due to infiltrated polymorphonuclears, macrophages, some erythrocytes, etc., and much nuclear débris. These areas may be fairly massive or insinuated between the muscle fibers. A few zones, distant from the rupture, show beginning organization (numerous fibroblasts and capillaries, and pigment-laden macrophages). Peripheral zones of hyperemia are conspicuous by their absence. Still rarer are the areas of true anemic necrosis, that is, where the outline of the muscle fibers is preserved, but all structural detail and nuclei are lost. The same picture of marked perivascular fibrosis is present here as in the other parts of the myocardium. Right ventricle: There are some changes in muscle fibers, but less marked. There is no marked fibrosis, though loose fibrous tissue and fat occur between the fibers.

*Histologic Diagnosis.* Coronary sclerosis and thrombosis, anemic infarct of myocardium; chronic interstitial myocarditis (perivascular). Organizing infarct.

*Comment.* The interesting features in this case are that rupture occurred during sleep, when there should have been the least amount of strain on the heart wall, and that it occurred in an unusual position, where the obvious chronic lesions were less advanced, but where the acute lesions were fraught with much greater danger, though not detectible by the naked eye. Although the myocardium grossly appeared the same as in many other localities, the microscopic picture clearly shows that following the recent coronary thrombosis (of at most a few days' duration), an anemic necrosis occurred, which offered less resistance than the more chronically injured tissue. From the obliquity of the tear it must have been, more or less, closed during systole, but allowed the blood gradually to escape during diastole until it so filled the pericardial cavity that the action of the heart was stopped. In regard to the supposed freedom from strain during sleep, MacWilliams has recently offered some interesting data which will be discussed later.

CASE II.—M. McB., aged about seventy years, a helper in the kitchen of this hospital, while at his usual work of peeling potatoes, complained of feeling badly, with a pain over his heart (May 26, 1924). A few minutes later he vomited and fell forward in his chair unconscious. His face became very blue, and his breathing stertorous. An intern who made a hasty examination could not hear his heart sounds at this time, and his lungs soon became filled with the coarse bubbling rales of pulmonary edema. He died less than five minutes after reaching the medical ward (Dr. Musser) and probably about fifteen minutes after his acute symptoms developed. Though elderly and rather feeble, previous to this he was not known to have been in poor health in any way.

*Autopsy.* (P. G. H., 8853, Dr. Eiman.) The pericardium extended 5 cm. to the right of the midline and practically to the ribs on the left. It contained 420 cc. of blood (partly in the form of currant-jelly clot).

The heart weighed 395 gm., measures 14.5 by 10 by 5.5 cm. and was of a peculiar, blunt, quadrangular shape. There were excessive amounts of pericardial fat, especially on the right side, the auricles were dilated, the ventricles contracted. A jagged, irregular tear, 7 mm. long, was found 3.4 cm. above the tip and 4.5 cm. to the left of the anterior coronary artery (that is, near the left border). The probe passed through this tear without any resistance into the left ventricle, where it was found to have traversed the split base of one of the mitral's papillary muscles. The myocardial wall, which here measured 11 mm. in thickness, was mottled brownish-red, with areas of brighter red and small irregular streaks of a tarry substance were found in their centers. The myocardium elsewhere was cloudy and brown in color. Its walls varied in thickness from 5 mm. at the tip of the left ventricle to 20 mm. in its thickest portion; the right ventricle was 5 mm. thick. The valve leaflets showed no noteworthy lesions; they measured as follows: Mitral, 9.3 cm.; aortic, 6.3 cm.; pulmonic, 7.5 cm.; tricuspid, 12.3 cm. The coronary arteries were greatly fibrosed and calcified; the anterior descending branch just above the site of the rupture had practically no lumen left, and was completely filled with red clot.

*Anatomical Diagnosis.* Hemopericardium. Acute suppurative myocarditis with rupture. Marked coronary sclerosis and thrombosis (?) of anterior descending branch. The other lesions noted were chronic fibrous changes in the pleura, spleen, kidney, pancreas and aorta, and a small right testicle with absence of left testicle and feminine body proportions and hair distribution.

*Histology.* Heart: Immediately beneath the normal epicardium and thick fatty layer the fibers (cut in cross-section) have a relatively normal appearance, except that in some areas there is considerable replacement with fibrous tissue. About 2 mm. deep there is a grossly visible blue staining zone, due to the occurrence of polymorphonuclear leukocytes and tissue débris, packed between the muscle fibers and grouped in circular areas. No bacteria can be found, even with special stains. The fibers here are narrowed by compression and either partly or wholly necrotic. For the remaining depth of the section (that is, as far as the endocardium), the muscle fibers, though not compressed, are wholly or partly necrotic and frequently surrounded by clumps of detritus and leukocytes. The Purkinje fibers are excessively prominent, swollen and apparently necrotic.

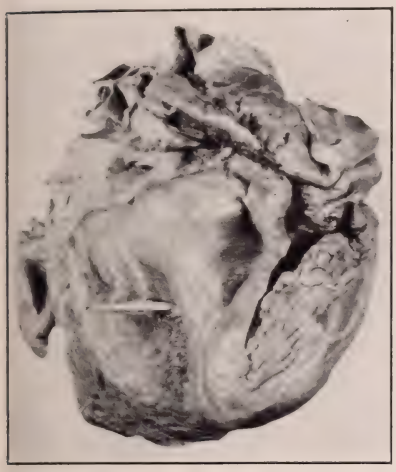

FIG. 1.—Case I showing rupture on posterior surface of left ventricle and surrounding pericarditis. The thrombosis of the descending coronary cannot be detected.

FIG. 2.—Case I showing oblique direction of tear with endocardial opening hidden behind the papillary muscle.

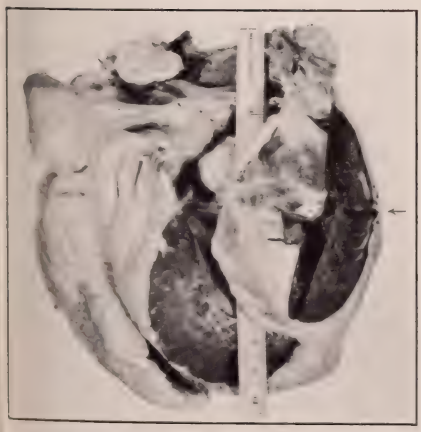

FIG. 3.—Case II with arrow pointing to line of rupture through wall of ventricle. Subepicardial hemorrhage is also shown

Fig. 4.—Case III, the ragged tear is seen joining the lower area from which section was taken.

*Histologic Diagnosis.* Acute infarct with liquefaction necrosis, due to coronary thrombosis.

*Comment.* The clinical history of this case is rather typical and illustrates some of the difficulties of proper study. Differential diagnosis from fatal coronary thrombosis would have been impossible. The absence of any known previous illness, especially in view of the lesions found, is noteworthy, though not infrequent.

The gross and microscopic signs of acute inflammation suggest that the heart may have been predisposed to rupture by bacterial suppuration; but in the absence of demonstrated bacteria and the presence of coronary thrombosis, it seems more probable that the necrotic infarct had liquefied and that the leukocytes were attracted by the sterile process.

Case III.—M. F., an obese Irishwoman, aged fifty-seven years, was admitted to the nervous department of this hospital on Dr. Pemberton's service on August 14, 1902, with the diagnosis of left-sided hemiplegia. There was nothing noteworthy elicited in her family and past history. Her present illness had come on during sleep, four weeks before, with inability to use her left arm and leg, but without speech disturbance. This condition had persisted without much improvement. Her pulse was rapid and sclerotic: there were no cardiac murmurs. Her urine was negative. On January 31, 1905, she went to bed feeling as usual. During the night the nurse noted that she had become cyanotic and that her breathing was stertorous and a few moments later she died.

*Autopsy.* (P. G. H., 440, Dr. Funk, twenty hours postmortem.) The pericardium contained a considerable amount of fluid and clotted blood. The heart was relatively small, weighing 350 gm. with a heavy layer of subpericardial fat. On the posterior surface of the left ventricle, 3 cm. above the apex, was a laceration, 15 mm. long and 5 mm. wide, parallel to the long axis of the heart. Near the rupture were numerous hemorrhages in the pericardial fat and a soft greasy yellow-pink area which occupied almost half the ventricle. The line of rupture was jagged and tortuous, reaching the endocardium just posterior to the base of the anterior papillary muscle. There was no evidence of scar tissue formation. The coronary arteries were markedly sclerosed. The lumen of the right coronary was especially diminished and contained clotted blood, which was probably an antemortem thrombus.

*Anatomical Diagnosis.* Hemopericardium. Rupture of posterior wall of the left ventricle, due to acute infarction (?) following coronary thrombosis. (At the time of autopsy this was termed local fatty degeneration.) There was also found cirrhosis of the liver and chronic parenchymatous nephritis.

*Histology.* Sections were not taken at the time of autopsy, but nineteen years later when the heart was first opened. Section of the posterior descending branch confirms the marked sclerosis with great narrowing of the lumen. Smaller branches near the rupture are totally occluded with dense fibrous tissue. The muscle adjacent to the line of rupture is much fragmented, and shrunken or wavy and disintegrated, with loss of striæ and nuclei. The areas of necrosis are not extensive, however. There is

no cellular infiltration, except for clumps of erythrocytes in the epicardial fat, and there is only a slight layer of fibrin almost free from cells. The muscle cells immediately adjacent to the line of rupture contain much golden pigment (hemosiderin?). There is considerable periarterial fibrosis.

*Histologic Diagnosis.* Coronary sclerosis and fibrous occlusion. Myocardial fibrosis with areas of necrosis.

*Comment.* This presents the usual clinical history and pathologic picture of coronary disease with myocardial degeneration, followed by thrombosis of a branch with infarction of the stricken area, and in turn by spontaneous rupture.

CASE IV.—M. K., an obese nervous white woman, aged fifty-eight years, was admitted to Dr. Burn's service of the neurological department of this hospital on August 27, 1923, with a diagnosis of right-sided hemiplegia. She complained of "nerves," and said she had had "neuritis" of her left arm and leg for two years. She denied any past illnesses, had had five children, two miscarriages and had a negative Wassermann reaction.

Physical examination showed the usual signs of an old hemiplegia, with equal pupils, partial aphasia and paralysis, and emotional instability. The heart dulness was slightly increased with a faint, apical, systolic murmur, not transmitted, and weak distant sounds. The urine showed a trace of albumin, but no casts and the blood chemistry was negative.

Except for persistent constipation, the patient continued the same for eight months, without any signs of cardiac decompensation. Suddenly at 1 A.M., while lying in bed, she became pulseless, very cyanotic and dyspneic, and died within fifteen minutes. When seen by the intern she was unconscious, though only fifteen minutes before the attack she was complaining merely of weakness and was somewhat dyspneic.

*Autopsy.* (P. G. H., 8772, Dr. Lucke, twelve hours after death.) The pericardial sac was distended with about 300 cc. of frothy clotted blood. The heart was of normal shape and somewhat enlarged, weighing 520 gm., and measuring 14 by 11 cm. There was much epicardial fat, varying from 4 mm. at the left apex to 8 mm. in thickness at the left base. Just above the tip of the right ventricle there was a slight bulging of the epicardium. due to a diffuse irregular hemorrhagic infiltration, roughly 4 cm. in diameter, Section here showed the epicardial fat to be 6 mm. thick over a thin strip of muscle, which varied from 1 to 2 mm. in thickness. In many places the fat extended into the left ventricular wall, especially in the bulging hemorrhagic area, where there was an irregular tear, 2 cm. in diameter, communicating with the right ventricle. The neighboring tissue was densely infiltrated with blood. The left ventricular wall averaged 23 mm. in thickness, but here thinned out to 6 mm. A walnut-sized thrombus adhered to the left apex. The chordæ tendineæ and papillary muscles were normal; the mural endocardium slightly thickened, especially below the aortic ring. The aortic leaflets had slightly stiffened, atheromatous bases, the valves otherwise being normal and measuring: Aortic, 8; mitral, 10; tricuspid, 12.5; pulmonary, 8.2 cm. The coronaries were somewhat tortuous and had an irregularly thickened intima. In the right coronary (the walls of which were much more diseased than the

left and were thick, distorted and crumbling), a firm red clot filled the lumen, beginning about 2 cm. from its origin. Both descending and horizontal branches contained the same kind of clot as far as could be traced. It was not possible to ascertain the primary site of thrombus formation. A branch from the main artery (given off before the main descending branch) was pointing straight for the rupture. This also was filled with red clot, but became too small to trace grossly before the rupture was reached. The muscle in this area did not vary grossly from the myocardium elsewhere.

*Anatomical Diagnosis.* Hemopericardium. Rupture of right ventricle. Coronary sclerosis with thrombosis of right branch. Hemorrhagic infiltration of apex with thinning of walls of both chambers. Antemortem clot in apex of left ventricle.

*Histology.* Large areas of fibrin, erythrocytes and cellular débris merge inextricably with muscle fibers in various stages of distortion and degeneration. In the less changed areas the muscle fibers are compressed between hemorrhagic infiltrates and numerous polymorphonuclears. There is marked evidence of scavenging and new tissue formation, with many phagocytes, plasma cells, eosinophils and beautiful "polyblasts," with relatively few new bloodvessels. The larger branches of the coronaries are much sclerosed and distorted and many filled with antemortem clot.

*Histologic Diagnosis.* Coronary sclerosis and thrombosis. Extensive necrosis of myocardium with beginning repair.

*Comment.* The rupture of the right ventricle accords with the thrombosis of the right branch. The extension of the necrosis into the left apex indicates that in this case the posterior descendens supplied more than its usual amount of myocardium. Correlation of clinical and pathological evidence shows that the coronary thrombosis (which from the histological picture must have occurred at least many hours before death) gave no signs or symptoms and that the terminal symptoms followed the actual rupture of the ventricular wall.

Case V.—A man, aged thirty-eight years, of dissolute habits, during a drunken debauch at Atlantic City fell heavily against a box for mixing mortar, hitting the edge against his precordial area. When seen by Dr. Henry Marvel, several days later, he had considerable precordial pain, but no diagnosis was made. No further details are now available except that death occurred suddenly.

*Autopsy.* (U. of P. Dept. of Pathology, No. 345.) The pericardial cavity was filled with clots of blood. About half way up the outer wall of the left ventricle in the visceral pericardium was a transverse tear, 3 cm. in length, which extended into the myocardium for about two-thirds of its depth. No mention is made of the coronaries grossly, but histologically the arterioles were reported as occluded and the myocardium near the rupture as acutely necrotic. (As Dr. Marvel's records were not available, the autopsy notes, supplemented by verbal statements of Dr. A. J. Smith, have been used with his kind permission.)

*Comment.* It is more probable that trauma played a prominent part in this case, but that it acted by injuring the coronary with subsequent

Fig. 5.—Case IV showing hemorrhagic infiltration and thinning of apex. Edge of the rupture is best seen in the tip of the reflected portion.

Fig. 6.—Case V showing transverse ragged tear 3 cm. in length, not penetrating into the cavity. Section has been taken in the middle of its upper border.

Fig. 7.—Case X showing the bulging hemorrhagic zone in left ventricle, from which various sections have been taken.

Fig. 8.—Case X, interior of left ventricle showing mural thrombus, subendocardial hemorrhage and great thinning of wall.

thrombosis formation and that rupture occurred "spontaneously" as a result of the thrombosis.

Case VI.—A housekeeper, female, aged sixty-five years, entered the Peter Bent Brigham Hospital at 9 A.M., and died suddenly at 5 P.M. She had had dyspnea for ten years and for more than a year had many attacks of sharp precordial pain, most apt to come on during excitement. Her chief complaint was of pain over the heart and in the stomach; she has had pneumonia but no rheumatic fever.

*Autopsy.* (P. B. B., No. 1744.) The pericardial cavity contained a dark purple clot which surrounded the heart like a cast. On removing this a small rupture of the left ventricle was found situated just to the left of the septum anteriorly, about 4 cm. below the base. This area of rupture measured about 1 cm. in length, was red and the margins fragmented. On the left side of the heart were numerous, rather fresh, friable mural thrombi situated over the lower half of the septum and apex, about the area of rupture. From the ventricular side this area of rupture gave the impression of a punched-out brick, which admitted the tip of the little finger halfway through the musculature of the heart. There were yellow and rather pale mottlings of the myocardium in this region, more suggestive of fat than of actual necrosis. There was no obstruction or narrowing of the orifices of the coronary arteries. On opening the anterior coronary artery which fed the area in which the rupture occurred there were several mural thrombi found on the intimal surface, the first being about 2 cm. beyond the orifice. Some of these were firmly adherent, paler and apparently considerably organized.

*Anatomical Diagnosis.* Coronary thrombosis. Rupture of myocardium of the left ventricle. Hemopericardium.

*Histology.* In certain areas the vessels are markedly congested and are surrounded by masses of blood. In these areas the muscle fibers are necrosed, and have among them a moderate polymorphonuclear exudate. This is apparently about the point of rupture. Numbers of small clumps of bacteria (pyknotic nuclei ?*) are also present here. The muscle fibers in other areas show a moderate degree of fragmentation.

*Comment.* The cause of rupture was evidently due to acute massive necrosis of myocardium caused by either embolus or thrombus.

Case VII.—A man, aged seventy-one years, the owner of a general store, entered the hospital complaining of pain in the epigastrium, of six weeks' duration. The pain radiated to the chest, usually lasted about three minutes and was sometimes relieved by rest. It bore no relation to meals. He had vomited three times. The last attack, which began on the morning of admission, began in the epigastrium and radiated to chest, right shoulder and arm. About two hours after physical examination the nurse found him gasping for breath and he stopped breathing shortly after.

*Autopsy.* (P. B. B., No. 19101.) The pericardial cavity contained 350 cc. of bloody fluid. About the auricle, posteriorly, were large masses

* Authors.

of clotted blood. The heart weighed 430 gm. On the anterior surface of the left ventricle, about 2.5 cm. from the apex and running downward and to the left, was an oblique linear rupture of the pericardium and myocardium just at the left of the interventricular septum, but visible on the endocardial surface, as only 1 cm. in length. The softened area about this rupture was supplied by the descending branch of the left coronary artery. About 2.5 cm. above the softened and discolored portions of the left ventricle this vessel was occluded by an atheromatous plaque which had become ulcerated with formation at that point of a dark red thrombus, about 4 mm. in length. No thrombi were demonstrable in other coronaries. The myocardium of the left ventricle in the softened area was found to be pale in several places, and particularly beneath the epicardium were several yellowish-white, irregularly shaped areas, from 2 to 8 mm. in size, suggesting anemic infarcts.

*Anatomical Diagnosis.* Infarction of the left ventricle with rupture and hemopericardium; thrombosis of descending branch of left coronary artery.

*Histology.* The cardiac muscle is degenerated and fragmented. At places it shows marked hyaline degeneration with infiltration of few leukocytes and fat globules.

*Comment.* None.

Case VIII.—A housekeeper, female, aged seventy-four years, on her first admission, which occurred a year previously, was discharged with a diagnosis of lobar pneumonia, thrombophlebitis and hypertension. She entered this time with a complaint of dyspnea. She had had two or three marked attacks of severe dyspnea and vertigo during the past year. On the day before entrance she was found sitting in a chair in an aphasic condition. A short time later a sharp pain was noted over the precordium. While in the hospital she suddenly began to cough, and died.

*Autopsy.* (P. B. B., No. 2164.) The pericardial cavity contained 150 cc. of bright red fluid and a large amount of blood clot. The heart weighed 410 gm. Over the anterior surface of the left ventricle and a portion of the right ventricle there was a reddish, granular exudate over an area about 5 cm. across, which was darker than the rest and surrounded a rent in the visceral pericardium which measured 3 cm. in length. This rent began 2 cm. below the pulmonary valve, and extended downward in a vertical direction. Upon making coronal sections a diffuse hemorrhage beneath the pericardium was found surrounding the opening. More coronal sections 3 cm. apart showed this rent to be an irregular slitlike opening, extending outward from the myocardium. It was located in the upper portion of the left ventricle in the tract of the anterior descending branch of the left coronary artery. The total area involved part of the anterior wall of the left ventricle and a portion of the septum downward to within 5 cm. of the apex. A small conical thrombus was found about 2 cm. below the origin of the anterior descending branch of the right coronary. In the wall of the left ventricle there was a large, adherent, friable mural thrombus.

*Anatomical Diagnosis.* Ruptured infarct of left ventricle. Thrombosis of anterior descending branches of the left coronary artery. Hemopericardium.

*Histology.* "The picture is that of necrosis superimposed on a myocardium with many cicatrices. There is very marked destruction of muscle in places with accumulations of polymorphonuclears and débris that give the appearance of abscess formation."

*Comment.* A typical case, with an interesting association with a probable cerebral thrombosis shortly before.

Case IX.—A man, aged sixty-three years, the superintendent of a dry-goods store, one year ago noticed that he occasionally was able to hear his heart beating somewhat irregularly. These attacks came on after excessive irritating and nervous work, and there was no associated dyspnea. He tired more easily than usual. He never noticed swelling in the feet or pain in the chest or other symptoms. Two weeks before admission the patient underwent some unusual strenuous exercise and the following day at 10.30 he suddenly felt a sensation of heaviness in the chest, unassociated with palpitation or dyspnea. It gradually became worse, and the patient was forced to pace about in agony, being unable to lie down. After continued pain in the chest and one very bad attack, he was admitted to the hospital, and died suddenly in the morning when raising himself in bed, after spending a comfortable night.

*Autopsy.* (P. B. B., No. 22100.) About 750 cc. of blood and blood clot was found in the pericardial cavity. Several light reddish-gray, somewhat friable clots, probably antemortem, were also present. There was a rent in the heart muscle on the anterior surface about 3 cm. from the left border of the heart and 8 cm. from the apex. The apex of the heart was soft and discolored. The heart, plus the clot, weighed 800 gm. (net, 700 gm.). The left ventricle was markedly dilated and had an aneurysmal dilatation at the apex, about 6 cm. in diameter. This dilatation was filled with a pinkish-red, granular, friable clot, evidently antemortem. The wall was extremely thin at this area, measuring 5 mm. in thickness. The thinning of the left ventricle began on the posterior wall, just below the attachment of the posterior papillary muscle. The intraventricular septum was apparently not involved. The left coronary artery had an arteriosclerotic lesion on the anterior surface of the heart about 1.3 cm. from its origin. At this portion there was a small pinkish-gray clot, about 1 mm. in diameter, probably a thrombus. The descending branch of the same artery was completely sclerosed a short distance from its origin. The right coronary was apparently normal.

*Anatomical Diagnosis.* Aneurysm of apex of the heart with mural thrombus. Rupture of the heart. Infarct of the heart. Hemopericardium. Obliteration of left descending coronary artery.

*Histology.* Some sections taken through the aneurysmal dilatation show extreme infarction of heart muscle, in which the entire musculature has been converted into a structureless débris, eosin staining, and in which are scattered nuclear fragments and an occasional polymorphonuclear leukocyte. In a section showing infarct and adjacent heart muscle, the fibers are pale, the nuclei are fragmented and some of the bundles of muscle fibers are necrotic and converted into a granular acid-staining débris. Between the muscle bundles is an increased amount of connective tissue. Young fibroblasts are seen in some areas. Dense scar tissue is also present.

*Comment.* This case offers an interesting correlation of clinical and pathological findings. Although the aneurysmal dilatation was infarcted, the actual rupture occurred slightly higher up.

GROUP II. *Coronary Sclerosis and Thrombosis with Myocardial Fibrosis Only.* CASE X.—G. S., a busy surgeon, aged sixty-two years, of good habits and health, complained for several days of pain in his upper abdomen, but it was not sufficient to stop him in his active practice. He had a good past history, except that he had been known to have a moderate amount of arteriosclerosis with hypertension for several years. He neither smoked nor drank. The morning of his death his discomfort was sufficient to keep him in the house, and soon developed into a "terrible oppression" in his chest, together with extreme restlessness, which persisted in spite of liberal doses of morphin hypodermically. This continued for about four hours, when he gasped and suddenly died.

*Autopsy.* (Presbyterian Hospital, No. 2, 1922, Dr. Eiman, after embalming.) The pericardial cavity was found distended to its utmost capacity with dark-red, soft, clotted blood. The heart weighed 420 gm., was rather pointed and contracted and measured 14 by 8.5 by 6.8 cm., and showed considerable subepicardial fat. On the lower anterior surface of the left ventricle, 3.5 cm. above the tip, was an irregular hemorrhagic area, 3 by 2.5 cm., in the center of which was a jagged rent, less than 1 cm. in length. A probe was passed without resistance into the left ventricle. On opening the left ventricle, at the angle of the septum and the anterior wall near the apex, there was found a soft, partly organized mural thrombus, measuring 6.5 by 2.3 by 1.8 cm. The portion of the wall to which the thrombus was attached was slightly bulging and concave. The inner aspect of the rupture was hidden in the mural trabeculæ, near the attachment of the thrombus, but was found to be smaller than the outer. The left ventricle was 5 mm. thick at the aneurysm, and 20 mm. at the base; the right ventricle, 7 mm.; the auricles, 1 to 2 mm. The myocardium was toughened and discolored by the embalming, but was firm and apparently normal. Even the thinner portion still had considerable muscle tissue left. The pulmonic valves were normal; the others slightly thickened.

The left coronary artery divided anomalously less than 1 cm. from its origin. The branches, which were almost parallel for several centimeters, were uniformly thickened and considerably calcified, but with ample lumina. Where the descending branch passed over the elevation of the base of the left ventricle its lumen suddenly narrowed to about 1 mm. in diameter and from there on was filled with a firm dark clot, which extended into the branch that supplied the ruptured area. This thrombosis probably occurred shortly before death. No thrombus was found in the right coronary. The valves showed no noteworthy lesions except for slight thickening along the edges of the mitrals, the bases of the aortic leaflets and diffusely in the tricuspids.

*Anatomical Diagnosis.* Hemopericardium. Rupture of left ventricle following thrombosis of the descending branch of the left coronary. Beginning apical cardiac aneurysm. Anomalous left coronary artery.

*Histology.* Muscular elements are surprisingly well preserved in sections from all chambers. The amount of perivascular fibrosis is moderate, about the same in all chambers and about what would be expected at sixty-two years. It is slightly greater in amount near the rupture. There is some perinuclear pigmentation. The main coronary branches show a disproportionate amount of sclerosis (more than the renal and much more than the aorta). Some lumina are filled with antemortem clot. Section from the edge of the rupture shows considerable hemorrhagic and some leukocytic infiltration but no evidence of necrosis. No ruptured fibers are seen in the section, and at this level the opening was caused by separation rather than rupture of the fibers. Section from the bulging thinned area shows pressure atrophy of the fibers, but surprisingly little degeneration and fibrosis.

*Histologic Diagnosis.* Marked coronary sclerosis and recent thrombosis. Perivascular fibrosis of myocardium. Pressure atrophy at dilated area and hemorrhagic infiltration.

*Comment.* In this case, in spite of the relatively small amount of perivascular fibrosis found microscopically, coronary disease was undoubtedly a factor in the beginning of cardiac aneurysm. The coronary thrombosis, though it was too recent to show any signs of organization, or even to cause visible changes in the myocardium, was apparently a factor in further weakening the myocardium to the point of rupture. The course of the anomalous coronary apparently predisposed it to sclerosis; what further influence the anomaly may have had is not determinable.

Case XI.—A housewife, aged sixty-one years, was admitted to the hospital, December 23, 1924, because she had been "out of her head" for the past twenty-four hours. History given by her husband: Mother died of diabetes, aged seventy-eight years; one sister had diabetes. Her past history was negative prior to the present illness, except for impaired hearing in the left ear in the last three years, associated with some earache and buzzing in that ear. Her present illness began two years ago with loss of weight (from 160 to 130 pounds in six months), increasing weakness, great thirst and hunger. Sugar was found in the urine. Her appetite was excessive and there was marked polydypsia. Three days before admission the patient became so weak that she went to bed. The second day before admission she became unconscious and the respirations labored. In the first nine hours following admission the patient received 120 units of insulin with some cereal and milk. The patient then seemed much better and was breathing quietly. She had a good night and in the morning seemed much improved. At 7.10 A.M., without any warning or noticeable distress, the patient died.

*Autopsy.* (P. B. B., No. 24100.) The pericardial cavity contained a large amount of blood clot, weighing 115 gm. The heart was distinctly enlarged and weighed 340 gm. On the posterior surface of the left ventricle, just to the left of the intraventricular septum, an irregular yellowish-white area of scar tissue was seen, 2 cm. in greatest dimension. In the center of this area was a slitlike opening in the heart wall, 4 mm. in length, with ragged edges. The heart wall surrounding the opening was repre-

sented by a layer of fibrous tissue about 2 mm. in thickness. On viewing the heart wall from within, a definite hole was seen in the myocardium, with ragged, necrotic edges, large enough to admit the tip of the finger. The right coronary artery at a point 3 cm. from its origin was occluded by a definite thrombus 8 mm. in length and grayish-red in color. This thrombus was evidently of recent origin. The artery was found to lead into the area of infarction described above, where its lumen was lost. The left coronary was negative.

*Anatomical Diagnosis.* Infarction of heart. Rupture of left ventricle at site of infarction. Thrombosis in right coronary artery (recent). Hemopericardium.

*Comment.* Another typical case associated with a cerebral lesion.

Fig. 9.—Case XII showing large, irregular "blow out" type of rupture.

Group III. *Coronary Sclerosis Only with Myocardial Fibrosis and Necrosis.* Case XII.—W. M., a man, aged seventy-four years, was admitted to the service of Dr. Riesman, in this hospital, October 16, 1911, with signs of heart failure. The brief history showed that he was a hard drinker and had had most of the contagious diseases but denied venereal disease. He soon developed severe precordial pain, acute dyspnea and cardiac arrhythmia, which progressed to true angina pectoris, Cheyne-Stokes respiration and death on the fourth day after admission.

*Autopsy.* (P. G. H., 2852, Dr. Ellis, eleven hours after death.) Autopsy showed 1100 cc. of blood in the pericardial cavity. The heart was fairly

large, weighing 570 gm., with a moderate amount of epicardial fat. On the anterior surface of the left ventricle near the septum, and 2 cm. from the apex, was a slightly angular tear, 7 mm. long, roughly parallel with the descending branch, with ragged edges discolored brown. Clotted blood was adherent and the muscle was friable. The wall of the left ventricle, which at the base was 2.3 cm. thick, measured 0.6 cm. at the apex, being thinned "almost to a membrane," and the cavity was dilated. It was a pale red color with yellowish spots, especially toward the apex. Trabeculation was marked, though the muscle columns were flat and stretched. The tear was at the upper edge of the pouch and not at its thinnest point. The coronary arteries were sclerotic, but the lumen was wide and partly filled with dark blood. No antemortem thrombus was found.

*Anatomical Diagnosis.* Hemopericardium. Rupture of left ventricle near dilated apex. Coronary sclerosis but no thrombosis.

*Histology.* There is a slight fleecy fibrosis between the fibers and, in patches, atrophy of muscle fibers with vacuolization and loss of longitudinal striæ. Areas of hemorrhage near the rupture vary with others of moderate round cell and polymorphonuclear infiltration. At the line of rupture the fibers are necrotic (wavy with total loss of nuclei and striæ). Many fibers terminate abruptly with ragged ends.

*Histologic Diagnosis.* Fibrosis and atrophy of myocardium. Necrosis and rupture of myocardium with hemorrhagic and cellular infiltration.

*Comment.* A good example of necrosis and rupture of the myocardium without coronary thrombosis. The coronary sclerosis was doubtless an important factor in the production both of the pouching and of the necrosis.

Case XIII.—A man, aged seventy-four years, retired, complained of shortness of breath and said his stomach rebelled against certain foods. A minute after the doctor left him the patient died.

*Autopsy.* (P. B. B., No. 1541.) The pericardial cavity was full of blood clot, which entirely surrounded the heart. On the posterior side of the left ventricle was a raised area, 2 cm. in diameter, which was slightly bluish in spots and showed one slit, 13 mm. in length, through which a probe could be passed into the left ventricle. Above this was the appearance of a slit, 5 mm. in length, but there was no aperture. There was marked degeneration of the muscle of the ventricular wall for a considerable distance on each side of the place of rupture. The coronary arteries showed a considerable degree of sclerosis and many places where the lumen was almost obliterated.

*Anatomical Diagnosis.* Rupture of left ventricle. Hemopericardium. Coronary sclerosis. Chronic myocarditis.

*Histologic Diagnosis.* Fatty degeneration. Necrosis and histolysis of the cardiac muscle.

*Comment.* Although the lumen of the coronary artery was not entirely obliterated, obstruction was sufficient to cause infarct and rupture.

Case XIV.—A housewife, aged forty-two years, complained of pain in the back for two weeks. Her past history was negative. Four days before admission the pain radiated to the left arm. On the day before

admission it was unusually sharp and lasted fifteen minutes. Physical examination showed a woman in much pain, rapid pulse and low blood pressure. She died after a week's stay in the hospital.

*Autopsy.* (P. B. B., No. 20104.) The pericardial cavity contained 250 cc. of bloody fluid and a large dark-red blood clot almost surrounding the right auricle. Several clots were present in the apex region of the sac. The heart weighed 400 gm. On the anterior surface, in the wall of the left ventricle, was a rent, 3.5 cm. long, extending obliquely downward to the left, at the beginning about 1 cm. to the left of the anterior branch of the coronary artery. There was a thin delicate deposit of fibrin about this, surrounding it in a zone about 4 cm. in width. An incision in the heart passing at right angles to this rent disclosed an actual defect in the wall as long as the linear lesion appearing on the surface, and about 4 mm. in width. There was here considerable loss of myocardial substance in the left ventricle, so that it was only 3 mm. in thickness in its greatest part. Filling this defect and about one-half of the ventricular space was a grayish-red thrombus, which had a relatively smooth surface. The remaining portion of the myocardium of the left ventricle measured 1.5 cm. in thickness, of a somewhat red cast with a few grayish-white lines, altogether suggesting fatty infiltration. The coronary arteries as a whole were markedly thickened, the right coronary showing great diminution of the lumen by calcification and atheromatous material concentrically arranged. Dissection of the left coronary showed much thickening of its wall along its entire length, and almost complete obliteration of the lumen of the main trunk. Histologically arteriosclerosis was rather generalized, but most marked in the artery where thrombosis occurred, with resulting infarction.

*Anatomical Diagnosis.* Rupture of the left ventricle of the heart, with thinning of its wall, due to infarction. Hemopericardium. Thrombosis of the anterior descending branch of the left coronary artery.

*Comment.* Infarction due to the coronary sclerosis had probably existed for at least several days before the rupture occurred.

Case XV.—A woman, aged sixty-three years, a practical nurse by occupation, had previously been at the hospital with diabetes and had frequent attacks of moderate dyspnea and palpitation with high blood pressure for many years. She came in the day before death, after having pain in the chest for six weeks, brought on by exertion. On the night before death she had severe pain beneath the sternum, radiating to the neck and shoulders.

*Autopsy.* (P. B. B., No. 21174.) The pericardial cavity contained 400 cc. of fluid which contained about 100 cc. of blood clot of recent formation. The fluid was thin and dark red. The heart weighed 400 gm. On the pericardial surface, about 4 cm. from the apex, in the region of the septum and the anterior descending branch of the left coronary artery, there was a slit about 3 cm. in length, through which blood oozed and around the margin of which there was discoloration for a distance of 8 mm. The slit was found to be 0.5 cm. from the septum and in the path of the above-mentioned coronary artery. There were also small adherent mural

thrombi. This was undoubtedly the place of rupture and the coronary leading to this area was more contracted than the other coronaries and showed more sclerosis, the lumen being definitely smaller. No actual thrombi or emboli were found. The other coronaries were patent and distended.

*Anatomical Diagnosis.* Rupture of the heart with infarct of the left ventricle. Arteriosclerosis of the anterior branch of the left coronary artery. Hemopericardium.

*Histology.* Sections from the left ventricle show considerable areas of hemorrhage and blood clot in the myocardium. The muscle bundles are large and present several areas of scarring, also foci of fat between the muscle bundles. Many of the muscle fibers show parenchymatous degeneration. One of the sections shows in addition considerable numbers of polymorphonuclears which have infiltrated the myocardium. The appearance is that of acute and chronic myocarditis with rupture of heart.

*Comment.* Again sufficient coronary obstruction was present to cause infarction without actual obliteration. Duration of the infarct is problematical.

Case XVI.—A man, aged seventy-two years, a cigar-maker, entered the hospital, February 26, 1925, complaining of pain in the chest. His family history was unimportant. For one year he had been troubled with nocturia, which had steadily become more annoying, so that for a few months he was forced to get up every half hour to urinate. For a few months he had complained of difficulty in starting urination, dribbling and burning micturition. Thirty-six years ago he had a chancre for which he received treatment with mercury, but subsequently a skin rash appeared which cleared on taking "black drops." In his present illness he had been dyspneic on slight exertion for several months. Occasionally he had been awakened at night with an attack of sharp substernal pain, which shot across the left side of his chest and down the ulnar surface of his left arm. These attacks occurred on exertion and sometimes made him feel an abnormal fear of death. Four days before entry, while sitting in a moving-picture house, he was seized with an attack much worse than any he had previously experienced. He went home and went to bed. The pain diminished considerably, but persisted in a milder degree until entry to the hospital. Except for frequency and dysuria, he was fairly comfortable until his fifth day in the hospital, when immediately after the use of a urinal he suddenly became pulseless, cyanotic and died almost immediately.

*Autopsy.* (P. B. B., No. 2537.) The pericardial cavity contained about 100 cc. of fluid blood as well as a large mass of blood clot lying between the two layers of pericardium. This clot weighed 420 gm. The heart was enlarged, weighing 500 gm., and was normal in shape. On the external surface and the posterior surface of the left ventricle, 1 cm. to the left of the intraventricular septum and about midway between the apex and the mitral valve, was a slitlike tear in the ventricular wall. This opening extended completely through the wall of the ventricle. On the external surface it was 2.5 cm. in length and 0.5 mm. in breadth, while on the inner surface it was about 1.5 cm. in length. The myocardium, radiating about

the rupture for a distance of 2 to 3 cm., was mottled, deep red and reddish-gray, and here the tissue was apparently more friable than elsewhere in the ventricular wall. The gross appearance was that of infarction. The left coronary artery, from its point of origin down to its bifurcation, showed considerable arteriosclerotic thickening of its walls, and in some areas its walls were calcified. The anterior descending branch, at a point 1 cm. below its origin, had a very rigid calcified wall, and its lumen was so narrow that it barely admitted the sharp point of the scissors. The circumflex branch of the left coronary artery showed similar calcification of its wall, and at a point 1 cm. from its origin was a calcified plaque on which a considerable amount of adherent grayish-red, friable blood clot was seen.

*Anatomical Diagnosis.* Infarction of the heart with rupture through infarcted myocardium (posterior wall of the left ventricle). Hemopericardium. Coronary arteriosclerosis. Hypertrophy and dilatation of the heart.

*Comment.* Typical for this group.

Group IV. *Coronary Sclerosis Only with Myocardial Fibrosis Only.* Case XVII.—M. M., a woman, aged seventy-six years, was brought by the police patrol to the Pennsylvania Hospital, April 23, 1914, with a clinical diagnosis of myocarditis. She had been sick for four days with epigastric and substernal pain, which at times had been severe. There was no history of dyspnea, edema, cyanosis or blood spitting. The heart sounds were weak and distant, but there were no murmurs. She arrived in "fair" condition, with some cough and pain in her left breast. An hour and a half later, before any further examination was made, she vomited slightly and suddenly stopped breathing.

*Autopsy.* (No. 1703, Dr. Bixby.) The pericardial cavity contained 500 cc. of fluid and clotted blood. On the anterior surface of the left ventricle, 1 cm. from the septum, and midway between the apex and base, was a linear opening, 15 mm. long, almost parallel to the septum, which communicated directly with the chamber of the left ventricle. On the external border were three irregular and quite superficial "cracks" in the pericardium. There was no sign of trauma. The heart weighed 270 gm., and had a moderate amount of superficial fat. The cavities were small. The muscle was very flabby and dark- red-brown. "At the point of rupture the left ventricle measured only 1 cm." (presumably it measured considerably more at neighboring points). The internal opening was smaller than the external and partly covered by the papillary muscle. The right ventricle was also soft and flabby; the aortic valves slightly thickened. "The coronary vessels are somewhat harder than normal, and can be traced quite readily beneath the pericardium."

*Anatomical Diagnosis.* Hemopericardium. Rupture of left ventricle. Brown atrophy. Coronary and aortic sclerosis. Chronic passive congestion of lungs and spleen, fatty liver, chronic interstitial nephritis.

*Histology.* The pericardium contains much fat and a coronary vessel greatly thickened with connective tissue rich in cells. The muscle fibers are shrunken and wavy, but not fragmented or vacuolated. The cross striæ are not seen. The nuclei are large and well stained with considerable

perinuclear pigment. The edge of the rupture is irregular with a thin layer of fibrin, and near the pericardium there is some infiltration with erythrocytes and leukocytes. There is considerable diffuse and focal infiltration of leukocytes, eosinophiles and lymphocytes. Some of the coronary arterioles are very thick walled, with almost obliterated lumen. Sections from the kidneys and liver showed several small collections of polymorphonuclears, and the spleen contained an unusual number of polymorphonuclears.

*Histologic Diagnosis.* Brown atrophy of the heart. Acute myocarditis. Splenitis, hepatitis and nephritis.

*Comment.* There is no evidence of coronary thrombosis or myocardial necrosis in this case, though the rupture seems to have been due to myocardial disease following coronary sclerosis. It is unfortunate that circumstances did not permit a more detailed study, so that the cause of the collections of polymorphonuclears and their relation, if any, to the rupture could be clarified. Their occurrence in organs other than the heart certainly suggests a pyemia which may have had an important connection with the rupture. The "cracks" in the pericardium are also of interest, even though their etiology and significance cannot be explained.

Case XVIII.*—A woman, aged sixty-eight years, who had been in poor health for years, had a "fatty heart" for a year. The day of her death she felt much worse and vomited. Four hours later she felt so badly that she had to lie down; but in a few moments sat up, retched, threw herself back, and was dead.

*Autopsy.* The pericardial cavity contained 8 to 10 ounces of blood. On the anterior surface of the left ventricle, 2 inches from the apex and $\frac{1}{2}$ inch from the septum, were two openings $\frac{3}{16}$ and $\frac{1}{8}$ inch long. On the internal surface one of these tears was hidden by a columna carnea. Grossly the heart did not seem fatty, but microscopically was said to be very fatty, the fibers breaking up longitudinally on slight violence. The aorta showed beginning sclerosis.

Further dissection, fifty years later, shows that the left coronary is greatly narrowed by a calcified area, 2 cm. from the aorta, before the descending branch is given off. It is also noted that the apex suddenly decreases from 1 cm. to about 3 mm. in thickness and is very fibrotic.

*Histology.* In spite of the great age of the material it is still possible to make out many histological details. For instance, near the apex the replacement of large areas of muscle fibers by dense bands of fibrous tissue, and in other areas definite perivascular fibrosis are easily made out. As striations and nuclei are not visible, it is impossible now to tell whether or not any acute necrosis was present. From its present appearance there does not seem to have been much fatty degeneration.

*Diagnosis.* Hemopericardium. Multiple rupture of the left ventricle. Coronary sclerosis with apical scar of old infarct.

* This case was reported by Dr. W. W. Keen in the *Transactions of the Philadelphia Pathological Society*, 1874–1875, v, 94, but is included here as opportunity has since offered to make a histological study.

*Comment.* This is a very good example of the kind of case which earlier passed as rupture due to fatty degeneration; but which in the light of later knowledge is found to have occurred in a heart that is the seat of marked

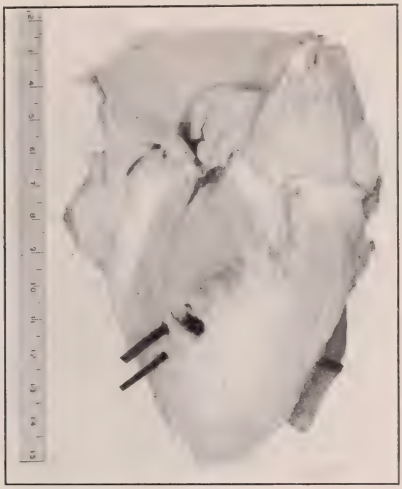

FIG. 10.—Case XVIII showing double rupture (with rods inserted) also place where section is taken. This specimen was fifty years old at the time it was photographed.

FIG. 11.—Photomicrograph of line of rupture of Case I.

coronary sclerosis with resultant thinning of the apex and replacement with scar tissue. Clearly coronary disease was an important factor in its causation.

Group V. *Coronaries not Mentioned.* Case XIX.—E. K., an Irish woman, aged seventy-four years, was admitted to the hospital, July 15, 1902, with a clinical diagnosis of myocarditis, complaining of joint pains for ten years. She had had the usual diseases of childhood. The short history described a fat, white woman, with a full slow pulse, muffled heart sounds, but no audible murmurs. On July 26 she died suddenly.

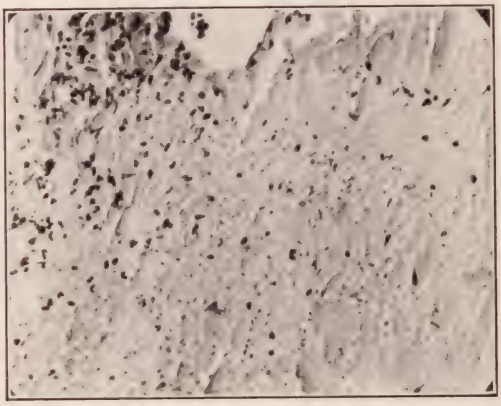

Fig. 12.—Photomicrograph of anemic infarct, following coronary thrombosis, with infiltration of red blood cells in the center of the picture and leukocytes at one edge. Case I.

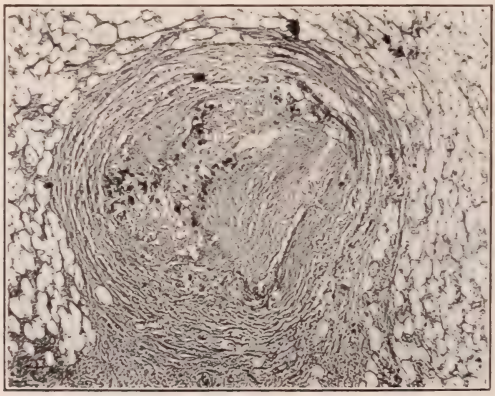

Fig. 13.—Photomicrograph of occluded branch of coronary artery. Case III.

*Autopsy.* (P. G. H., 5855, Dr. Coca.) The autopsy showed 300 cc. of blood in the pericardial cavity. The heart, which weighed 400 gm., was pale and friable and had considerable epicardial fat. At the auriculo-ventricular junction on the anterior surface of the left ventricle was a tear, the walls of which were infiltrated with blood so as to form a swelling, 2 cm.

in width, extending along the auriculoventricular groove. The mitral valves were fatty and sclerotic. The aorta showed moderate sclerosis, but the coronaries were not mentioned. There was no histologic report.

*Anatomical Diagnosis.* Fatty degeneration and rupture of left ventricle.

*Comment.* The paucity of evidence in this case makes it impossible to tell if this was really fatty degeneration or an infarction following occlusion of the left coronary.

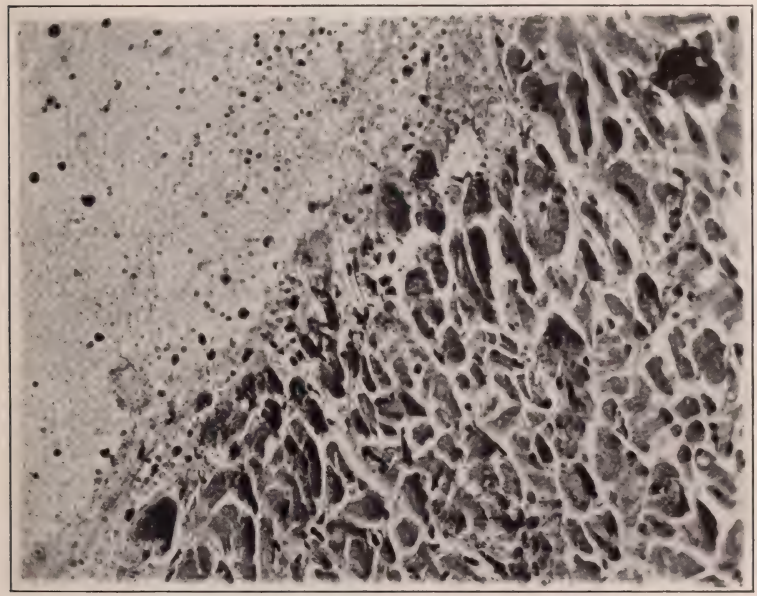

Fig. 14.—Photomicrograph of edge of rupture of Case III, showing hemosiderin granules in muscle cells along edge.

Case XX.—E. F., a white woman, aged sixty-four years, was admitted to the neurological service of Dr. Potts, September 14, 1901, with a hemiplegia of two years' standing. She was also aphasic and incontinent both of urine and feces. She also had a large ulcerating carcinoma of the breast and axilla. The only mention of the heart was that the second aortic sound was rough. The urine was negative. She died December 5, 1902.

*Autopsy.* (P. G. H., 5981, Dr. F. P. Gay.) Autopsy showed a large well-nourished woman with the aforesaid cancer. The pericardial cavity was found full of blood, and the surface of the heart covered with fibrin. The apex was firmly adherent to the parietal pericardium by fibrous adhesions. When the fibrin was removed two ragged openings were found on the anterior surface extending through the copious fat into the cavity of the left ventricle. The coronaries were not mentioned. Histologically, there was much fragmentation and segmentation and perinuclear pigmentation, more marked in the right auricle than in the left ventricle. The diagnosis was made of brown atrophy.

*Comment.* As the section taken was obviously not from the neighborhood of the rupture, it is not possible to say what the condition of the myocardium was at this point. The apical adhesion suggests an organized infarct, which in turn suggests coronary disease. The occurrence of further coronary occlusion with rupture of the resulting anemic infarct is at least as probable as any other explanation.

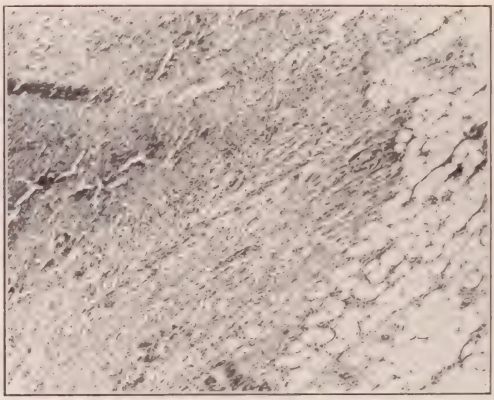

FIG. 15.—Photomicrograph of Case IV showing cellular infiltration in myocardium and epicardial fat and polyblastic connective tissue formation.

FIG. 16.—Photomicrograph of extensive myocardial fibrosis, Case XVIII.

CASE XXI.—A clubman, aged sixty years, and a moderate drinker, came to the office of Dr. B. F. Stahl one morning about 8 A.M., complaining of precordial pain. Very little was known about his general condition, except that he said that he was seldom sick. After a short examination which revealed nothing startling, he was sent home, where he died suddenly in about an hour. There was loss of sphincter control just before death.

*Autopsy.* The pericardial cavity contained much blood, which was found to have come from several small tears in the lower third of the left ventricle, some of which communicated with its cavity. No further details of the condition of the heart are available.

*Comment.* None.

CASE XXII.—A. U., an aged female, died at the hospital, October 29, 1868, after having been insane nineteen years. She was a very large, fat, flabby woman, with a weak heart, some cough and dyspnea, but no edema. The day of her death she complained of pain in her left side. That evening she suddenly fell over, and died in a few minutes.

*Autopsy.* (P. G. H., 72.) The pericardial cavity contained 12 ounces of dark blood and clot. The heart was not much enlarged, weighing 14½ ounces, but was unusually flabby and covered with a fatty deposit. One inch from the apex of the anterior surface of the left ventricle, near the septum, was a tortuous irregular rent, ⅓ inch long, on the endocardial surface and partly filled with firmly adherent clot. Its edges were rough and agged and the external fibers seemed more torn than the internal. The coronary arteries were not mentioned.

*Histology.* Marked fatty degeneration of the muscle fibers either with central loss of transverse striæ or complete loss of striation with granular degeneration. Only a few healthy fibers remained.

*Comment.* This seems more like rupture due to fatty degeneration than any case of the series, and yet in the absence of more detailed statements, especially about the coronaries, the question must be left undecided.

CLINICAL AND PATHOLOGICAL DATA. The figures for the age, sex and site of rupture and, to a lesser extent, for survival after rupture are based on all of the 654 cases. The remaining items are based almost entirely on the cases abstracted by us. It is perhaps unnecessary to add that the items that we have attempted to investigate were completely reported by very few and in many cases only a small number were mentioned.

CLINICAL. *Sex.* Three hundred and four were males and 217 were females. This corresponds fairly well with the generally accepted view that males are slightly more prone to the accident, though Quain stated that in his series the two sexes were equal in this respect. He gave no actual figures. The predominance of the causes of arteriosclerosis in the male sex is doubtless responsible. In statistics of coronary sclerosis the preponderance of males is more marked.

TABLE I.—SEX DISTRIBUTION.

| | Our analysis. | Quain. | Minet. | Robin. | Total. | Per cent. |
|---|---|---|---|---|---|---|
| Male . . | 185 | Considered | 38 | 81 | 304 | 58.3 |
| Female . | 112 | Equal | 37 | 68 | 217 | 41.7 |

*Age.* The average age at which rupture occurred was well in the sixties. The greatest number of cases occurred in this decade and the next greatest number in the seventies. When one considers how few persons relatively live to reach this age the results are truly astonishing. These figures confirm the opinion that spontaneous rupture of the heart is characteristically and strikingly a phenomenon of old age and suggest the fundamental importance of the condition of the coronaries. Particular interest attaches to the underlying cause of rupture in those patients who died young, and, as one might expect, coronary disease no longer plays a predominant role. Of the 25 cases in our abstracted series under forty years there were 17 males to 8 females. Acute infection was a prominent factor in 9, lues in 5, trauma in 4, alcohol in 3, coronary disease in 2 and 3 doubtful. The auricles were more prominently involved; the left, 5 times; the right, 4; the right ventricle, 2; the left ventricle, 13; multiple tears, 2.

TABLE II.—AGE DISTRIBUTION.

| Decennials. | Our analysis. | Quain. | Minet. | Robin. | Tota. | Per cent. |
|---|---|---|---|---|---|---|
| Aged | 24 | .. | .. | 6 | 30 | 4.9 |
| 80+ | 12 | 6 | 13 | 21 | 52 | 8.6 |
| 70's | 63 | 24 | 22 | 58 | 167 | 27.7 |
| 60's | 99 | 33 | 19 | 37 | 188 | 31.3 |
| 50's | 47 | 13? | 8 | 13 | 81 | 13.4 |
| 40's | 25 | 6? | 4 | 8 | 43 | 7.1 |
| 30's | 12 | 25 { 3 | 2 | 6 | 23 | 3.9 |
| 20's | 4 | 2? | .. | .. | 6 | 1.0 |
| 10's | 5 | 1? | 2 | .. | 8 | 1.4 |
| 1 to 10 | 4 | .. | .. | .. | 4 | 0.7 |
| Total | 295 | 88 | 70 | 149 | 602 | |

*Habits, Occupations and Predisposing Causes.* Pertinent statements about these items were obtained in less than one-quarter of the cases abstracted by us. All social classes were subject to attack. Forty-seven of them were insane, a remarkably high incidence that has been noted by others and for which we have no explanation other than the common factor of arteriosclerosis. Except for this and the frequency of intemperate habits (noted in 24 cases), it cannot be said that these items of our study contributed much of interest or value. Even the notation of intemperance is subject to two general fallacies underlying statistics, namely, that a comparison with intemperance in subjects whose hearts did not rupture is not feasible and that possibly the authors' attentions may have been unduly focused on this point. Syphilis was conspicuous by

its rarity, except in those dying under forty years. Twelve were noted as obese, though this number should undoubtedly be much higher.

*Exciting Causes.* These are manifold in the coronary cases and vary from severe to the slightest form of exertion: Eating, 14 cases; walking, 13; defecation, 10; while conversing, 5; getting out of bed, 6; emotional excitement, 5; at toilet, 5; trauma, 3; convulsions, 3; attack of angina, 3; violent exertion, 2; sitting up in bed, dressing and so forth, 9. Five were, as far as they knew, perfectly well until they suddenly fell over dead. Twenty-one died during sleep (including 1 of our own series), but according to recent work of MacWilliams, this is not a period as free from strain as one might suppose. Particularly during dreams or restless sleep he found marked changes both in the rhythm of the heart (heart block, etc.) and in the blood pressure (increase of 20 to 30 mm.), which might easily be sufficient to rupture a necrotic myocardium.

*Premonitory Symptoms.* Attacks of vertigo, cough, dyspnea, syncope and even hematemesis are said to be indicative of the prodromal stages of rupture. They were not at all conspicuous in the case reports we studied and certainly not more so than would be found in the equal number of several cardiac cases whose hearts did not rupture. Diarrhea and vomiting seemed to have somewhat more significance. Anginal pain, on the other hand, was obviously important, being noted 70 times (in 7 out of 9 of the Boston cases), but this should be interpreted rather as a sign of coronary disease than of impending rupture. We know of no way accurately to differentiate the two conditions from the point of view of this symptom. In fact it may be said that the early symptoms are chiefly those of coronary disease and that it is still impossible to predict which cases of coronary disease are to suffer rupture. In a fair number of cases no preliminary symptoms preceded the acute attack.

TABLE III.

| Survival. | Our analysis. | Quain. | Minet. | Robin. | Total. | Per cent. |
|---|---|---|---|---|---|---|
| "Sudden" . . . | 178 | 71 | 31 | 8 | 288 | 72.0 |
| Less than 10 min. | 30 | .. | 1 | .. | 31 | 7.7 |
| 10 min. to 20 min. | 7 | .. | 1 | .. | 8 | 2.0 |
| 20 min. to 1 hr. | 3 | .. | .. | .. | 3 | 0.8 |
| 1 hr. to 12 hrs. . | 14 | .. | 18 | 2 | 34 | 8.5 |
| 12 hrs. to 48 hrs. . | 7 | .. | 10 | .. | 17 | 4.2 |
| 2 days to 8 days | 3 | .. | 10 | .. | 13 | 3.3 |
| 8 days . . . . | ... | .. | 6 | .. | 6 | 1.5 |
| | 242 | 71 | 77 | 10 | 400 | |

*Terminal Symptoms.* Death is usually so sudden that in many cases the person is seen merely to fall over dead or is found dead. This applies to the auricular as well as to the ventricular cases. In a single case, where the physician chanced to be at the patient's bedside when the rupture occurred, a peculiar rushing, roaring sound was heard through the stethoscope that had been immediately placed over the patient's precordium. If life lasts a few moments there are signs of acute collapse, with air hunger, pallor or deep cyanosis, with stertorous breathing, cold sweat, perhaps vomiting, convulsions or unconsciousness, and in the few cases in which the heart has been ausculted the sounds are faint but rhythmic, or absent and the radial pulse imperceptible. In the rarer type lasting a few hours or more the patient may have the usual signs of acute cardiac failure, cough, angina or increasing signs of chronic heart failure. The time that the patient survived after the rupture had taken place is given in Table III, as well as it can be estimated. But the reader must realize that this table is no certain picture of the facts. In several cases where death was reported as occurring so many days to weeks, and even, in 1 case, to over a month after rupture, consideration of the history and actual course of symptoms reported lead us to the decision that the time given for the first occurrence of rupture really indicated a situation arising from sudden occlusion of a coronary, while the actual rupture probably took place at a much later date. In these cases we have taken the liberty of tabulating the period of survival according to our own interpretation of the symptoms, rather than after the original report. At the present time, after more careful study of the histologic sections taken from our own cases, we feel that we have perhaps erred in these later interpretations of symptoms, and that some of these cases may really have survived longer than we thought possible. The wide infiltration of blood and leukocytes, and in some cases even an apparent attempt at connective tissue formation, are conditions that take more than a few minutes to produce.

*Mechanism of Death.* This is still far from clear, but probably varies with the size of the rupture and the consequent suddenness with which the pericardium is distended and the rest of the system deprived of its normal supply. For obvious reasons it is practically always impossible to make an accurate study in clinical cases. One might assume that cardiac arrest from the increasing pressure from the overdistended pericardium must play an impor-

tant part, especially in the slow leaks that survive for some hours; but as Robin and Nicolle point out, some patients die with very little blood in the pericardium and cases of traumatic rupture are known to survive for a longer time than the spontaneous cases. On the other hand, Vance has recently shown in cases of traumatic rupture that if the escaped blood can drain into the pleural cavity death may be postponed for many hours. A second factor, especially in the sudden cases, is cerebral anemia, but to be so suddenly fatal the cerebrum must be deprived of more blood (perhaps by vasomotor action) than that lost into the pericardial cavity. The terminal symptoms in some cases resemble those of fatal coronary thrombosis, where presumably cardiac arrest is primary; but others are more like those of cerebral syncope. Disturbance of cardiac mechanism, such as ventricular fibrillation, must also be taken into account.

TABLE IV.—SITE OF RUPTURE.

| | Our analysis. | Quain. | Minet. | Robin. | Total. | Per cent. |
|---|---|---|---|---|---|---|
| Right auricle | 20 | 7 | 2 | 6 | 35 | 5.7 |
| Left auricle | 8 | 2 | .. | 2 | 12 | 2.0 |
| Right ventricle | 32 | 13 | 5 | 13 | 63 | 10.2 |
| Left ventricle | 225 | 78 | 70 | 120 | 493 | 79.7 |
| Miscellaneous | 7 | ... | .. | 8 | 15 | 2.4 |
| Totals | 292 | 100 | 77 | 149 | 618 | |

PATHOLOGIC. *Site.* The site of the rupture was mentioned in almost every autopsy report. As will be seen in Table IV, the left ventricle greatly predominated and especially on its anterior surface. In Minet's and our series the anterior surface was involved 150 times as against 57 of the posterior, 38 of the apex and 5 of the external surface. Of 60 cases in which the location was further specified, the rupture was in the lower third in 35, in the middle third in 21 and the upper third in only 10. In traumatic cases, on the other hand, the left ventricle is less commonly involved than the right, on account of its less exposed position.

The right ventricle is a poor second. Of the 32 cases of our series the anterior surface was involved 14 times (upper third, 1; middle third, 3; lower third, 6; not mentioned, 5); the lower third of the posterior surface, 2; the apex, 6; site unmentioned, 9.

The right auricle was ruptured 35 times (equally distributed over its various parts); the left only 12 times.

The 15 miscellaneous ruptures of the table were of the septum,

apex (unqualified), or where the chamber was not designated. The reason for the predilection of the anterior surface of the left ventricle is chiefly that it is the descending branch of the left coronary that is most markedly atheromatous and most frequently thrombosed. The greater pressure in this chamber is undoubtedly an important contributing factor both to the rupture and to the greater amount of sclerosis. Discussion of the reason for the greater damage to the anterior coronary is hardly within the scope of this inquiry. As far as we know it has not been determined, but presumably the firmer support of the posterior surface by surrounding tissues would play a part.

It is noteworthy that the average age of those dying from rupture of an auricle was much less than that of the ventricular cases. In our series only 6 out of 25 cases of auricular rupture were over sixty years, with an average age of forty-three years, and in Robin and Nicolle's, 4 out of 10 with an average age of forty-seven years. The non-coronary origin of the early deaths has already been discussed and of course the same factors apply here as well.

*Character of Tear.* In 223 cases in which the size of the rupture was given 60 (27 per cent) were less than 1 cm. in length, 5 of these were just large enough to admit a probe and 20 were less than 5 mm. in length. Sixty-four (28.7 per cent) were between 1 and 2 cm. in length; 43 (19.3 per cent), between 2 and 3 cm.; 24 (10.8 per cent), between 3 and 4 cm.; 17 (7.6 per cent), between 4 and 6 cm.; 15 (6.6 per cent), between 6 and 8 cm. The width (mentioned in 10 cases) varied from 2 to 25 mm., with an average of 8 mm. In 25 out of 36 cases the internal opening was given as smaller than the external; in 9 it was larger and in 2 equal.

The nature of the tear was mentioned in 166 cases and varied considerably. The edges were irregular or jagged in 72, clean cut in 20 and infiltrated with blood in 24. Linear tears were frequent, and described as oblique in 22, longitudinal in 18, transverse in 2, tortuous in 9, curved in 4, angular in 3, oval in 5, triradiate in 4, valvular in 1 and in 1 the apex had been pathologically amputated and lay free in the pericardial cavity.

The great majority (269) of cases were complete ruptures of a wall of the heart, producing large hemopericardia. In 8 of these, however, there was no mention of fluid blood or clot in the pericardial cavity. In 1 this was due to the rupture extending through an adherent diaphragm to the abdominal cavity. Presumably most of the others were the omissions of an incomplete report.

Reports of partial ruptures were for the most part discarded. However, to get some idea of their usual position and cause, the first 16 cases met with were preserved. Of these, 4 were ruptured septa and 6 were papillary muscles. Of the other 6, 1 was a ruptured parasitic cyst (without blood in the pericardium); 1 showed separation of the auricular fibres without actual rupture (small amount of blood in pericardium); 1 ruptured into a coronary vein; 3 of varying depths from the pericardial surface did not reach the heart chamber (all showing blood in the pericardium).

TABLE V.—APPARENT EXCITING CAUSES.

| | Our analysis. | Quain. | Minet. | Robin. | Total. | Per cent. |
|---|---|---|---|---|---|---|
| CONDITION OF CORONARIES GIVEN. | | | | | | |
| Coronary thrombosis | 74 | 6 | 51 | 24 | 145 | 23.8 |
| Marked coronary disease with various myocardial lesions | 68 | 1 | .. | 44 | 113 | 18.5 |
| Cause not determinable, coronaries approximately normal | 9 | .. | .. | 2 | 11 | 1.8 |
| CORONARIES NOT MENTIONED. | | | | | | |
| Cause not determined | 41 | .. | 10 | 17 | 68 | 11.1 |
| Heart apparently normal | 4 | .. | .. | 1 | 5 | 0.8 |
| Fatty degeneration and infiltration | 59 | 77 | 15 | 35 | 186 | 30.4 |
| Softening* | 18 | .. | .. | 24 | 42 | 6.8 |
| Thinned walls (aneurysm and fibrosis) | 28 | .. | .. | 4 | 32 | 5.2 |
| Syphilis | 3 | .. | 1 | 1 | 5 | 0.8 |
| Tuberculosis | 1 | .. | .. | .. | 1 | 0.2 |
| Parasitic cyst | 1 | .. | .. | 1 | 2 | 0.4 |
| Tumor (melanotic sarcoma) | 1 | .. | .. | .. | 1 | 0.2 |
| | | | | | 611 | |

* This group includes indefinite descriptions such as apoplexy, red softening, ulceration, gelatinous degeneration, etc. Doubtless many were really infarcts, others merely flabby or fatty and a few true abscesses.

*Underlying Cause.* The investigation of the cause underlying the rupture was considered by us to be one of the most important topics of the inquiry; but the incompleteness of many of the pathological reports has made it one of the least satisfactory. Thus, early impressed with the importance of the condition of the coronaries in this respect, we examined each report carefully for a statement about them, and yet in 156 out of 307 cases they are not mentioned—a fault by no means confined to the earlier observers. In fact even in the 22 cases now reported by us for the first time, in 4 it was impossible to get a statement about the coronaries. In Table V is given the results as best they can be tabulated, in the face of such difficulties. The largest group—fatty degeneration—

is recruited chiefly from the older cases and undoubtedly contains many—perhaps even a large majority—that today would be given different and more accurate designations.

Of the 151 cases of ruptured heart in which the condition of the coronaries is mentioned, they are said to be more or less diseased in all but 9. This would perhaps be expected where the average age is so high, but assumes a different and important aspect when coupled with the fact that in 74 cases actual thrombosis of the coronary had occurred and that in 32 more the coronary disease was sufficiently severe to cause either marked thinning of the ventricular wall (with or without aneurysmal dilatation, 20 cases) or acute or chronic myomalacia (organized infarct, 8 cases). Of the remaining 29 cases, coronary disease was associated with fatty degeneration in 12; sclerosis, brown atrophy and so forth, in 8; no other condition mentioned in 9.

In 157 cases the condition of the coronary arteries was not mentioned. In these cases also it was, of course, more difficult to appreciate the exact condition of the myocardium, on account of differences in terminology and conception of disease a generation ago. Thus "fatty degeneration" was a very popular term, which, based on gross inspection only, was probably frequently used incorrectly to describe acute infarction as well. In this group, for instance, it occurred 59 out of 157 times (37 per cent), while in the first group only 19 out of 151 times (12.6 per cent), 7 times associated with coronary thrombosis and 12 times with other forms of coronary disease. Continuing with the second group, "ulceration" was the assigned cause in 8 cases, and we suspect that this included some cases of infarct; infarct, as such, was given only 7 times. In 23 cases the ventricular wall was described as locally thinned to such a degree that it was obvious that the condition at least approximated cardiac aneurysm following coronary disease. Among the other assignable causes were fatty infiltration, 6 cases; fibrosis, 5 cases; syphilis, 3 cases; abscess, 3 cases; brown atrophy, 2 cases; parasitic cyst, tuberculosis, melanotic sarcoma, each 1 case. In 41 cases no cause was assignable, and in 4 the heart musculature was said to be normal. Without adequate histologic examination, however, this statement is of little value, and spontaneous rupture of a normal heart wall is properly questioned.

What a different picture these figures give from the usual textbook description of the underlying pathologic lesions of ruptured

heart! Consideration of the two groups permits the conclusion that spontaneous rupture of the heart wall is due in the great majority of cases to antecedent coronary disease, often with actual thrombosis, causing either an acute infarct (acute myomalacia) or organized infarct or such a poor state of nutrition that the muscle fibers degenerate and the thinned wall stretches to form a cardiac aneurysm. In the latter case rupture seems to occur either with or without a terminal necrosis of the muscle fibers. The small remaining minority is to be accounted for chiefly by acute and chronic infectious processes.

*General Condition of the Heart.* Apart from the condition of the myocardium at the site of the rupture, the most striking feature was the excessive amount of subpericardial fat, which was especially noted in 58 cases and was a prominent feature in most of the cases personally observed by us. It is noteworthy that the myocardial fibers were usually better preserved just beneath the pericardium than they were at other levels. So-called fatty degeneration was noted 34 times and the heart called pale and flabby (and often greasy), 25 times. Brown atrophy was noted 7 times; myocardial degeneration, 6; myocarditis, 4; fibrosis, 4. The heart was usually said to be enlarged. In 34 cases in which we have noted the weight, it averaged 433 gms. (270 to 870 gms. as extremes).

Discussion. It seems, then, that a person dies from a broken heart, not in young adult life from a great grief or emotion, but usually in old age, on account of diseased coronaries and from such immediate prosaic causes as walking, eating, defecation, slight exertion, or even during sleep. The condition was first described, as far as we can learn, by William Harvey, who also observed precordial pain in his patient and at autopsy found "an impediment to the passage of the blood from the left ventricle into the arteries." Morgagni (who himself died from it) described it in an old woman, aged seventy-five years, who had the traditional fatty heart. Among its distinguished victims were George II (during defecation, Elleaume), Morgagni, the Scotch Dr. Abercrombie, Admiral Villeneuve, who after his defeat by the English was said to have committed suicide by lacerating the right auricle with a needle introduced between the ribs.

The underlying causative agents are reasonably well known, though it is far from clear why following coronary thrombosis, for instance, some infarcts should rupture and others go on to organization. The exciting causes also show a dissatisfying diversity that

can only be partly accounted for by our inability to say exactly when the rupture occurred. One would naturally think that the accident would be especially associated with conditions causing increased intracardiac pressure; yet granted that this may occur at such unlikely times as during sleep, as has been previously suggested, still many other cases occurred after quite trivial movements or during absolute rest. Presumably the progress of the necrosis plays a more important part (compare our second case with liquefaction necrosis), though apparently in some cases the functional weakness may be operative before the usual microscopic signs of necrosis are visible (Case X).

The actual method of production of the rupture is still open to discussion. Apparently some ruptures progress from the inside out and more *vice versa*, depending on which zone or layer the most necrotic and weakest focus happens to be in. From the postmortem appearances most are produced suddenly with rapid outpourings of blood (is this begun in systole or diastole?); but some, with sinuous, thrombin-covered walls, undoubtedly have progressed much more slowly.

The symptomatology is not characteristic and difficult to separate from that of coronary thrombosis, and the time available for study is usually very short. The diagnosis is therefore seldom made antemortem, and doubtless many cases of sudden death in the aged have had unsuspected ruptures. Terminal progressive increase of precordial dulness might in rare cases permit a correct diagnosis. In a few cases it has been made before autopsy, if not before death.

This is of no great matter, however, as the prognosis of a complete rupture is, as far as we know, invariably bad, and no method of treatment has been found to be of any use. It is, of course, possible that very tortuous minute passages might be blocked spontaneously by a clot long enough to permit organization or adhesion to the parietal pericardium to take place, and this possibility becomes more probable in the partial tears. As regards surgical intervention, in view of the diseased state of the myocardium, it is hardly conceivable that suture would be of any use, even if the correct diagnosis were made in sufficient time.

Study of the morbid anatomy brings out several interesting moot points. The posthrombotic infarct, the organized thrombus, septic foci and so forth need not be further discussed here. The

frequent concurrence of marked fatty deposit in the pericardium is curious, but its relation to the rupture obscure. The great diversity in the character of the tear and the variable relative size of the internal and external openings are indications that the mechanism of rupture differs in different cases, but offer no clue to solve this question. Another curious observation is that the internal opening has not infrequently been found partly hidden behind a papillary muscle, where it would seem to be relatively well protected. The case in which rupture occurred in an area supplied by a recently thrombosed artery, but not showing visible signs of necrosis (our Case X) indicates that functional weakness can be manifest before signs of structural change. It must be recognized also that coronary thrombosis may occur without signs or symptoms, that considerable myocardial necrosis may occur without coronary thrombosis (Cases XII–XVI) and that following coronary thrombosis the myocardium may at autopsy appear normal, even to the trained pathologist, and yet histologically show considerable necrotic and infiltrative changes (Case I).

Some of these questions will undoubtedly be solved by future clinicopathologic observations; others can perhaps be better attacked by carefully planned animal experimentation.

Summary. From analysis of 22 cases hitherto unpublished, and 278 cases reported by others, and from a survey of 354 further cases from the literature (totaling 654), the following conclusions may be drawn:

Spontaneous rupture of the heart is chiefly an accident to the left ventricle of the aged; in the aged it is practically always due to coronary disease. It most frequently occurs in an acute infarct of the anterior surface of the left ventricle following sudden thrombosis of an artery or one of its branches; or less frequently the infarct may follow gradual fibrotic occlusion of the lumen.

With severe coronary sclerosis and consequent myocardial degeneration (usually with more or less cardiac aneurysm), rupture may occur in an area not obviously necrotic and supplied by a patent artery. The bursting of a cardiac aneurysm has been observed, but is rare. Evidence is presented to show that the formerly popular diagnosis of fatty degeneration is usually incorrect or open to serious question.

Other rarer causes of spontaneous rupture considered in this analysis are "ulceration," fatty infiltration, fibrosis, syphilis,

abscess, brown atrophy, parasitic cyst, tuberculosis, melanotic sarcoma. Most of these are based on reports of little value on account of the antiquity or incompleteness of the data.

Evidence about the site and character of the tear is considerable and accurate, but the actual mechanism which produces rupture and the actual cause of death are not clearly understood.

All classes and occupations are liable and the exciting causes are most diverse. Premonitory symptoms are frequent but not characteristic. Terminal symptoms are usually so abrupt that little treatment can be even attempted and the antemortem diagnosis is seldom made.*

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## DISCUSSION

Dr. Bowman C. Crowell: The continued satisfactory action of the myocardium depends upon the integrity of a number of factors, and Dr. Krumbhaar has shown us how it depends upon the integrity of the coronary system and coronary circulation. We know a considerable amount now about the coronary diseases. Of the end-results we know more than we do of the earlier results, and it is this most tragic effect of the end-results that Dr. Krumbhaar has described this evening. In his description he has referred to those cases which show fat infiltration, and it seems to me it is possible to interpret that fat infiltration as itself an evidence of a coronary sclerosis as it occurs in old people. That amount of fat in old people, I

* Very similar findings are reported by F. R, Nuzum and H. J. Hagen, Spontaneous Rupture of the Heart, Am. Jour. Med. Sci., 1926, clxxi, 185.

think, is seldom found without some grade of coronary sclerosis. It is possible that may be the interpretation of it. We can trace practically all the results of cardiac disease in the myocardium through the different stages, as has been mentioned by Dr. Krumbhaar: The earlier stages, where there is insufficiency of circulation with degeneration of the heart muscle and atrophy of the heart muscle and its replacement by fibrous tissue, at times with actual infarction of the heart muscle, occurring without thrombosis and healing without formation of scars, sometimes with dilatation into aneurysm, in which case the result may be sudden explosion of the heart. In these cases treatment is seldom of any avail. In the first place, these cases rupture at times when treatment is not available, and even if one is able to make the diagnosis and go in, it would be practically impossible to sew up a heart which is in the condition in which these hearts are found.

I have seen at autopsy a heart which had been sutured some years previously, but it was unfortunate that the individual who had that heart contracted tuberculosis. It was a traumatic rupture from stabbing. The individual contracted tuberculosis and the pericardium was so involved with tuberculosis that it was impossible to even recognize the scar in the myocardium.

The effect of coronary disease differs in different individuals and that may depend upon the fact that the coronary circulation is not always the same. The anastomosis of the different coronary vessels has been shown to be very different in different individuals, and it is a question whether that factor of the anastomosis present in the individual concerned will be one of the factors in determining the site at which rupture of the heart takes place. It would be interesting to know, in these cases in Dr. Krumbhaar's series in which a rupture took place on the right side of the heart, whether there had been some extra strain on the right side of the heart caused by such a condition as pulmonary obstruction or something of that kind.

There is just one other feature I would like to mention, and that is that it is always interesting to me to note the distribution of arteriosclerosis. Why some individuals should have sclerosis of the coronary vessels without sclerosis of other vessels, why others have cerebral sclerosis, others renal, and others general arteriosclerosis is puzzling. What the factor is that determines the arterial sclerosis in the vessels in different areas is yet to be discovered.

Dr. Krumbhaar (closing): In regard to Dr. Crowell's remarks, there is only one of our series that occurred on the right side, an old woman with hemiplegia, around Blockley for sometime, and she was not considered to have serious heart disease and had no apparent strain on the pulmonary circulation.

# PURPURA HEMORRHAGICA (THROMBOCYTOPENIC PURPURA) WITH REPORT OF A CASE WITH SPLENECTOMY*

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Sir William Osler[1] referred to purpura as "that obscure and interesting manifestation of which we know so much and at the same time so little." Since Osler made this reference much has been done to properly classify conditions accompanied by purpura. The present-day conception of the classification and diagnosis of primary purpuric disease still resembles, however, the state of the conception a number of generations ago of intermittent fever. Knowing the exact etiology of malaria as we now do, we can project the probable fact that patients suffering from intermittent fever of pyogenic origin were grouped together with patients infested with the plasmodium of malaria and considered as having an identical disease. Atypical cases of malaria without intermittent fever no doubt escaped true classification.

Aplastic anemia, purpura hemorrhagica and acute myelogenous leukemia may show clinical signs and symptoms of very similar character—an acute downward fatal course, hemorrhages from mucous membranes, purpuric eruption, reduction of blood platelets, prolonged bleeding time and profound anemia. In the majority of cases final classification into one of the three groups is possible. But borderline cases occur where the exact diagnosis must remain in doubt, even in the presence of collected evidence from history, physical examination, clinical laboratory data, and postmortem examination of tissues. No one at the present time is able to say, definitely, whether these three diseases are or are not related. E. Frank, the distinguished German hematologist, believed primary

* Read May 6, 1925.

aplastic anemia and purpura hemorrhagica to be the same disease. Others equally distinguished are of a different opinion.

In the year 1731, Werlhof[2] separated purpura hemorrhagica from the general group of purpuric diseases. Hayem[3] in 1889 emphasized the observation, published by Denys[4] two years previously, that the blood platelets were present in markedly decreased number in a case reported by Denys. Since that time nosologists have shifted their point of view from the manifestation, *purpura*, to the manifestation, *reduction of blood platelets*, in their attempt to arrive at a proper classification. This has led to the coining of a number of new names for the condition, which no doubt will be discarded in turn when the final etiology of the entity is arrived at. The disease probably occurs in mild form without the manifestation, reduced blood platelets, and without purpuric spots.

Wright made the observation in 1906 that blood platelets are derived from the pseudopodia of the megakaryocytes of the bone-marrow. No one has successfully disputed this finding since that time and gradually it has been accepted. Much remains unknown, however, concerning the origin and physiology of these peculiar bodies.

In 1915 E. Frank[5] arrived at the conclusion that the blood platelets are *always* reduced in purpura hemorrhagica and proposed the name "essential thrombopenia." In 1920 Eppinger[6] suggested that essential thrombocytopenia was a better term as directly pointing to reduction of the platelet cells rather than the substance thrombin. Hayem noted the extraordinary fact that there is an absence of clot retraction in primary purpura hemorrhagica. Duke[8] in 1912 emphasized the prolonged bleeding time in the presence of a normal coagulation time in this disease.

Theories of pathogenesis of primary purpura hemorrhagica have been many and interesting. Certain French writers[9] held that disturbances in hepatic function were primarily at fault. Grenet's work[10] indicated that a toxic action on the central nervous system was the primary factor. The theory of infection has had many advocates. Giffin and Holloway[42] state: "There is a growing conviction that it (purpura) is usually secondary to localized infection and that in some way chemical toxins are formed as the result of bacterial action which affect the vascular tissue." They suggest that the process is not due to the direct action of a bacterium or its products,but to a secondary abortive substance originally designed to protect, the process probably being linked with protein intoxication.

Primary changes in the walls of the capillaries have been demonstrated in experimental purpura. In 1914 Ledingham[49] produced purpura with hemorrhagic symptoms by injecting animals with antiblood-platelet serum. Bedson[11] concluded from observations on experimental purpura in 1922 that the two main factors concerned in the production of hemorrhages in purpura are (1) toxic action on the endothelium of bloodvessels; (2) removal of platelets from the circulation.

Recently Bedson[43] has investigated the effect of splenectomy upon the blood platelets in experimental purpura. He states that splenectomy in guinea-pigs gave rise to a great increase in the number of blood platelets in the blood stream. Blood platelets reached their highest level in ten to fourteen days and declined to normal in three or four weeks. Bedson concludes that splenectomy cannot be relied on to give any but temporary relief in the treatment of purpura hemorrhagica. This is especially important in view of the recent literature on splenectomy as a curative measure in purpura hemorrhagica.

Frank[14] formulated a theory in 1915 that hemorrhages in primary purpura were due to an inhibitory action of the spleen on the bone-marrow causing a reduction of the number of blood platelets in the circulation. Kaznelson[16] agreed with Frank that the spleen was concerned in the reduction of blood platelets in hemorrhagic purpura, but thought its action was a destructive one on the platelets after formation rather than an inhibition of proper formation. Brill and Rosenthal[13, 41] have suggested that the entire so-called reticulo-endothelial system is concerned in the reduction of the number of blood platelets, the reticulo-endothelial tissue of the liver, lymph nodes and elsewhere participating, as well as that of the spleen.

The treatment of primary purpura hemorrhagica has included efforts by local and general styptic drugs to combat hemorrhages, injection of serum, injection of foreign protein, roentgen-rays over the spleen and bone-marrow and recently the operation of splenectomy. In 1916 Kaznelson[16] reported brilliant results following splenectomy in a case of thrombocytopenic purpura hemorrhagica. Since that time approximately 50 patients[13, 42] have been splenectomized for this condition in various parts of the world. The majority of these reports are confirmatory of the value of this procedure.

Case Report.—E. M., aged eighteen years, a schoolgirl, was admitted to the Pennsylvania Hospital, Philadelphia, on November 4, 1924, on the

service of Dr. Charles F. Mitchell. Her chief complaint was bleeding from the vagina and gums. For the past ten months she had felt generally weak and had been told by relatives that she was pale. For the past two months she had been bleeding at intervals small amounts from the gums; and for the past five weeks she had been bleeding from the vagina. About a month before admission a large number of purpuric spots appeared on the skin. These lasted for a long time, but disappeared. Her appetite was poor. Her bowels were constipated. She had had repeated attacks of sore throat during the past few years.

*Physical Examination.* The patient is a well-developed, well-nourished girl, but very pale and seems to be extremely anemic. Bleeding from the gums is the only positive finding about the head. There is no adenopathy. Examination of the lungs shows nothing abnormal. The heart is negative except for a soft systolic murmur at the apex. The spleen and liver are not felt and there are no masses or areas of tenderness. She is bleeding and passing clots from the vagina.

On account of the possibility of incomplete abortion, a dilatation and curettage was done on the day of admission. Blood clots were evacuated, but the patient continued to bleed. There was no evidence on examination of curettings of an abortion.

Shortly after this a diagnosis was made of purpura hemorrhagica.

Dr. George W. Norris made the following note on consultation on November 12: "Blood-pressure 117/55. Small pea-sized pale bluish-red petechial spots on left groin. Several brownish spots on back, smaller and may have had similar origin. Constriction of brachial vessels by blood-pressure cuff for about two minutes, sufficient to cut off circulation has not produced petechia. Several petechial spots over right inner lower biceps region. Pain and tenderness right lower abdomen. Spleen not felt, not enlarged to percussion. Lungs clear. Heart not enlarged. Soft low-pitched systolic murmur at apex of heart. Liver not felt except in epigastric notch. I believe this is a case of purpura hemorrhagica and, in view of recent literature, splenectomy might be considered."

*Course of Disease.* On November 12: Transfusion—300 cc. whole blood, direct method. The patient continued to bleed. The transfusion improved her general condition but she did not stop bleeding from vagina. The bleeding from the gums has practically stopped.

November 15: Transfusion two hours before operation of 475 cc. of whole blood. The spleen was removed. It was found to be somewhat enlarged and adherent to the diaphragm. The tail of the pancreas was also adherent near the hilus of the spleen. There was very little oozing. The patient's pulse became quite rapid during the operation, reaching 170 per minute, but remained of fair volume. She reacted well from the operation.

She was considered to be in such good condition after coming out of ether that a postoperative transfusion was not done.

November 17: Given 35 cc. of whole blood intramuscularly. The patient has continued to bleed from the vagina since operation about the same as before. Bleeding from the gums has ceased.

November 19: Transfusion of 400 cc. of blood.

The patient's general condition improved after each transfusion, but bleeding continued from the vagina.

November 21: The uterus packed with gauze soaked in thromboplastin.

November 21: Several small purpuric spots have appeared under the left breast.

November 22: Bleeding has stopped from vagina since packing.

November 22: 700 cc. whole blood transfused.

November 23: Her temperature has risen to 106° F. (rectal), pulse 120. No bleeding from uterus.

November 24: Her temperature rose this P.M. to 105° F. (rectal); pulse-rate, 120. There is a systolic murmur at the apex; the abdomen is soft, with no tender points or masses. The operative incision is in excellent condition. She has been incontinent all day, passing bowel movements and urine in bed frequently.

November 28: Great numbers of purpuric spots have appeared over the whole body. The tourniquet test is positive. There is no bleeding from the uterus and most of the packing has been removed. The patient is extremely anemic and the effect of blood transfusion lasts but a day or two.

November 29: Transfusion of 400 cc. of citrated blood did not produce a reaction and the patient died shortly after.

*Laboratory Work.* The Wassermann test was negative. Analyses of urine showed albumin present, varying from a trace to a heavy cloud, with no sugar or casts. Both aërobic and anaërobic blood cultures were made. On November 12 blood cultures were negative. On November 28 a rod-shaped organism, was seen in a Wright's stain of the blood. Blood cultures taken immediately showed the Bacillus fecalis alkaligines in both aërobic and anaërobic cultures. It may be interesting here to note that this organism was found also postmortem in cultures from the vena cava.

Clotting time on November 7 was seven minutes. On November 17 it was four minutes; November 28, four minutes. Oxidase stains made both before and after operation showed the abnormal mononuclear cells present to belong to the myeloblastic series. The red blood cells both before and after operation showed polychromatophilia, some poikilocytosis and anisocytosis and occasional stippling.

BLOOD COUNTS

| Date | Red blood cells, millions. | Hemoglobin per cent. |
|---|---|---|
| November 4 | 3,000 | 35 |
| November 7 | 1,160 | 25 |
| November 11 | 0,945 | 25 |
| November 16 | 1,270 | 25 |
| November 17 | 1,035 | 25 |
| November 18 | 1,043 | 25 |
| November 19 | 0,786 | 20 |
| November 21 | 0,730 | 20 |
| November 21 | 1,650 | |
| November 24 | 1,480 | 25 |
| November 28 | 1,100 | 20 |

WHITE BLOOD COUNTS

| Date. | Total count, per c.mm. | Differential count in per cent. | | | | | | Nucleated reds per c.mm. |
|---|---|---|---|---|---|---|---|---|
| | | Poly. | Lymphо. | L. M. | Tr. | Eos. | Myelocytes. | |
| November 4 | 9,600 | 31 | 32 | 2 | 4 | 0 | 31 | 0 |
| November 7 | 5,200 | 33 | 28 | 2 | 1 | 0 | 36 | Occasional |
| November 10 | 9,400 | 27 | 8 | 4 | 1 | 0 | 54 | 0 |
| November 17 | 40,000 | 56 | 4 | 2 | 3 | 0 | 35 | 45,000 |
| November 18 | 37,000 | 50 | 7 | 1 | 2 | 0 | 40 | 43,000 |
| November 19 | 54,000 | 43 | 7 | 1 | 0 | 0 | 49 | 36,000 |
| November 20 | 34,000 | 52 | 1 | 0 | 2 | 0 | 45 | Many |
| November 21 | 20,400 | 45 | 10 | 2 | 1 | 0 | 42 | 47,000 |
| November 22 | 23,236 | 46 | 9 | 0 | 0 | 0 | 45 | 39,564 |
| November 23 | 55,000 | 42 | 3 | 0 | 0 | 0 | 55 | 105,000 |
| November 24 | 24,950 | 66 | 3 | 2 | 1 | 0 | 28 | 80,850 |
| November 26 | 36,000 | 90 | 2 | 0 | 0 | 0 | 8 | 24,000 |
| November 28 | 53,000 | 62 | 2 | 0 | 0 | 0 | 36 | 7,200 |

BLOOD PLATELET COUNTS

| Date. | Per c.mm. |
|---|---|
| November 11 | 40,000 |
| November 14 | 30,000 |
| November 16 | 80,000 |
| November 17 | 70,000 |
| November 18 | 70,000 |
| November 19 | 64,000 |
| November 24 | 90,000 |
| November 26 | 130,000 |

Examination of the feces was negative except for a stong reaction for occult blood. There was no frank bleeding from the lower bowel.

Bleeding time on November 7 was twenty minutes; on November 15, thirty minutes; on November 17, four minutes; on November 27, twenty minutes.

Clot retraction was absent both before and after operation. The blood when allowed to remain several days in the ice-box showed no retraction of clot.

*Examination of Spleen Removed at Operation.* The spleen is moderately enlarged, weighing 190 gm. Its surface is smooth and glistening. The capsule does not appear to be thickened. The cut surface is uniform in color. There are no gross nodules or areas of localized involvement. The pulp is of brick-red color and lies even with the cut surface. The reticulum grossly shows no apparent increase in amount.

Microscopic sections show no thickening of the capsule. The trabeculæ are prominent and distinct, but there is no evidence of increased amount of fibrous tissue in the spleen. The germinal centers are distinct. The blood spaces are filled with cells having the morphological appearance of myeloblasts and myelocytes. The arrangement or lack of arrangement of these cells suggests that they are transient cells. There is no evidence of the uniform hyperplasia of cells *in situ* with destruction of architecture so characteristic of the myeloid hyperplasia of myelogenous leukemia. The lymphocytes and lymphoblastic cells of the germinal centers show no

evident deviation from normal morphology. No blood platelets can be distinguished.

*Postmortem Findings.* (Dr. J. R. Paul) The body is that of a well-developed and well-nourished young Italian girl. There is a very marked pallor of the skin and mucous membranes. Scattered over the chest and abdomen are showers of purpuric and ecchymotic spots. These are present over the breast, upper abdomen and anterior surface of the arms. The legs are more or less free from these spots, although there are two present over the femoral triangle on both sides. There is a recent T-shaped surgical incision in the left middle quadrant of the abdomen (both arms measuring about 15 cm. in length). It is fairly well healed, but the edges are hemorrhagic and serum oozes from it.

The examination is confined to the surgical incision.

Peritoneal Cavity: On opening the peritoneal cavity it is found to be free from blood, although parietal and visceral peritoneum are studded here and there with tiny ecchymotic spots. An extremely interesting condition is encountered in that there is a well-developed sac of peritoneum situated on the left side of the peritoneal cavity, the orifice of which is opposite to Treitz's fossa. Fully two-thirds of the small bowel is loosely enclosed in this sac. As the duodenum and jejunum emerge from Treitz's fossa they enter this sac and the gut in this region is small, extremely pale and collapsed. Its contents are small in quantity and pale pink. In striking contrast is the appearance of the small gut as it emerges from the sac. It becomes distended, the walls are extremely dark and the contents dark red. There is no evidence of incarceration or strangulation. The colon is somewhat dilated throughout. All of the mesenteric lymph nodes are tremendously enlarged and edematous, some are cherry-red in color, others are pale red, varying in size from that of a pea to an olive. This includes the glands in the mesentery, about the celiac axis and along the spinal column. In contrast the glands in the pubic region and mediastinum are not enlarged. In the region of the splenic flexure (spleen removed) there is a large collection of broken-down blood. Most of it seems to be retroperitoneal in location and situated about the tail of the pancreas.

The lungs and heart are examined through the diaphragm.

Heart: Definite cardiac hypertrophy is present.

Lungs: Pulmonary edema, mild in extent, is present in both lower lobes.

Stomach, Duodenum, Pancreas: No gross changes noted.

Intestines: As noted above.

Liver: The liver is of normal size and appearance except for pallor.

Adrenals: The adrenals are small and pale orange in color. No hemorrhages.

Kidneys: Both kidneys present the same picture. They are quite large. The surfaces are smooth and pale. On section the cortex is found to be quite thick, extremely pale and the renal architecture poorly defined. The picture is that either of extreme anemia or acute parenchymatous degeneration and infiltration of white cells.

Pelvic Organs: The uterus is small and of normal shape and size. It is

dark red in color. The walls and cervix are soft. On exposing the uterine cavity a dark semigangrenous endometritis is encountered. Both ovaries are enlarged. The tubes are normal. The bladder is normal.

*Autopsy Sections.* Pancreas: The islands appear to be somewhat hypertrophied. The capillaries and other blood spaces contain blood showing many myeloblastic cells and nucleated red cells. No other noteworthy changes.

Liver: The capsule shows no changes. The liver cells appear shrunken. Some contain fat droplets. The capillaries are dilated and contain blood with a high percentage of myeloblastic cells. There is an occasional small area of perivascular exudation of cells of the same type seen in the blood stream. These resemble more an inflammatory reaction than the infiltrative areas usually encountered in leukemia.

Adrenals: Section is not remarkable. Bloodvessels contain myeloblastic cells.

Kidneys: Sections show very few changes except cloudy swelling of the tubular epithelium. The glomeruli, bloodvessels and interstitial tissue are not particularly abnormal in appearance. There are no focal collections of cells.

Small Intestine from Hernial Sac: The changes are not striking. Several dilated lymphatics are present in the submucosa. The bloodvessels are dilated with myeloid cells.

Uterus: Sections show erosion of the mucosa with congestion and vacuolization of the epithelial cells of the glandular acini. The uterine veins are dilated and in places filled with plugs of blood and fibrin containing large numbers of polymorphonuclear and myeloblastic cells. There is no definite infiltration of interstitial structures with myeloblastic cells.

Mesenteric Lymph Node: The capsule is not thickened. The architecture of the node is largely preserved. There is marked edema. The marginal and septal sinuses are filled with red blood cells, nucleated red cells, myeloblasts and lymphocytes with a few large phagocytic cells enclosing red cells, mononuclear cells and debris. The pulp shows the same picture as that detailed above except for more abundant fixed cells of lymphocytic type. The uniform hypertrophy of abnormal cells seen in the leukemias is not present.

Bone-marrow: The bone-marrow is quite cellular. There is no evidence of fatty infiltration or replacement. The cells are largely myeloblasts, erythroblasts and occasionally megakaryocytes, with some red blood cells containing no nuclei. Occasional phagocytic cells are seen containing ingested débris and cells. The impression one gets is that the mother cells of both the red cells and the polymorphonuclear cells are quite active and hyperplastic.

Summary of Findings. An eighteen-year-old girl was admitted to the hospital with a history of purpuric spots on the skin two months previously. Purpuric spots were present during stay in hospital and constriction of arm with blood-pressure cuff produced purpuric spots. For two months before admission she had been bleeding small amounts from the gums. For five weeks before admission she bled more or less continuously from the vagina.

She developed extreme anemia, but her general nutrition remained good and there was very little emaciation. None of the supreficial lymph nodes were enlarged. The spleen was not particularly enlarged. There were no signs of cardiac or pulmonary disease or evidence of localized infection.

Bleeding time was prolonged. There was marked reduction of blood platelets. Coagulation time was normal. Clot retraction was absent. Anemia was profound. Before blood transfusion three counts of white blood cells ranged from 5200 to 9600; a differential count showed myeloblasts and myelocytes present. These were interpreted as a symptomatic myeloblastic stimulation from strain of repeated hemorrhages on bone-marrow.

A splenectomy was done after preliminary blood transfusion.

Following splenectomy the patient ceased to bleed from gums. Vaginal bleeding continued until the uterine cavity was packed. After operation repeated transfusion of whole blood was done. The effect of raising the hemoglobin and red cell content of the blood was only temporary, though there was no gross evidence of red-cell destruction such as jaundice.

The patient died apparently of anemia and exhaustion despite repeated transfusions. After splenectomy there was an enormous increase of nucleated red cells with a large number of leukocytes of myelobalstic origin.

Discussion. The question of the proper diagnosis of this case presents some difficulty even in the presence of fairly detailed clinical history, laboratory results and postmortem findings. The patient presented the cardinal signs and symptoms of thrombocytopenic purpura: (1) Purpuric eruption; (2) hemorrhages from gums and vagina; (3) marked anemia; (4) prostration; (5) absence of a definitely localized area of disease to account for the condition; (6) prolonged bleeding time; (7) normal coagulation time; (8) marked diminution of blood platelets; (9) absence of clot retraction.

The unusual feature, however, was the presence of myelocytes and promyelocytes in fairly large relative proportion.

Ordway and Gorham[48] state: "A diagnosis of acute myelogenous leukemia in order to be above criticism must be substantiated by proof of the following points: (1) An aleukemic or subleukemic stage; (2) an acute downward course with death usually in from one to four months; (3) the characteristic picture of myeloblasts and myelocytes with transition forms between the two; (4) typical gross and histological findings in the liver, spleen, bone-marrow and lymph glands; (5) specific proof of myeloid elements by enzyme reactions (oxidase stains)."

In regard to Item 4 they say: "A slight myeloid change is not sufficient proof. It must be a marked transformation, since mild

proliferation of myeloid tissue is not uncommon in severe anemias. The possibility of error in failing to insist upon this point is well illustrated by Naegeli."[47]

Myeloid changes in the tissues of the case under discussion were not striking. The picture was not at all typical of the usual myeloid hyperplasia of leukemia. The myelocytes and myeloblasts present in the kidney, spleen, lymph nodes and liver were largely contained in bloodvessels and blood spaces. The uniform hyperplasia of myeloblasts in the enlarged lymph nodes with destruction of architecture so characteristic of the leukemias was entirely lacking. Stimulation myelocytosis in severe anemias, especially acute and subacute types of severe anemias, is a comparatively common finding. Examples might be multiplied of this type of myelocytosis in severe anemias with subsequent complete recovery of the patient.

We have felt, therefore, that it is impossible to classify the case as acute myelogenous leukemia and feel that the case was one of severe essential thrombocytopenic purpura with marked stimulation myelocytosis.

Consideration of the question of why the patient failed to recover after splenectomy is of speculative interest and may afford some practical points. Transfusion of blood was not done immediately after the operation. Brill and Rosenthal consider that blood transfusion should immediately precede and follow the operation. It was not immediately done after operation by us because of the apparently good condition of the patient and because we considered the transfusion immediately preceding the operation to have been sufficient.

After operation the patient stopped bleeding from the gums, but continued to bleed from the vagina until the uterus was packed. It is possible that local measures to control vaginal bleeding should have been taken earlier. We hesitated to do this because of the danger of infection and because we hoped day after day that bleeding from the uterus would stop.

The theory of Brill and Rosenthal[41] that the entire reticuloendothelial system is involved in platelet destruction, that in the lymph nodes, liver, and elsewhere as well as the spleen, calls up the speculation as to whether in very severe cases, such as the one under discussion, sufficient of the offending system is not removed by splenectomy to stop the process.

The finding of the jejunal hernia is of interest. Its significance

is not apparent. While the patient had no clinical signs of intestinal obstruction the well-known intensity of reaction from the absorption of toxic products from an obstruction to the higher portions of the bowel makes this fact of the hernia of enough speculative interest to be mentioned in a discussion of the case. It is possible that the immediate origin of the organism isolated from the blood (Bacillus alkaligines) was from the partially imprisoned loop of small bowel, and that the retrogression following the temporary post-operative improvement may have been due to absorption of toxins from this area. Certainly the microscopic appearance of the mesenteric lymph node lends support to this view.

As we watched the blood picture from day to day we were struck by the profound struggles of the bone-marrow to replace red blood cells in the circulation, as witnessed by the enormous number of nucleated red blood cells. Lenoble[44] believed he had discovered a new form to which he gave the name of myeloid purpura. This was characterized by the presence of a considerable number of normoblasts in the circulating blood. In the acute stage of the disease the number varied between 165 and 1250 per c.mm. In 1 case he found 3000 per c.mm. Sometimes, according to Lenoble, neutrophilic myelocytes and more rarely eosinophilic myelocytes are found in the blood during a myeloid reaction. Labbé and Ameuille[45] concluded from their study that there was nothing specific in the myeloid reaction. It varied with the extent of the hemorrhage and disappeared when bleeding ceased.

The number of nucleated red blood cells in our case after splenectomy reached the enormous number of 105,000 per c.mm. We have not found in the literature any case approaching this figure. Before splenectomy was done there were only a few nucleated red cells, although the anemia was almost as profound at times before operation as after it. It certainly seemed that removal of the spleen profoundly stimulated the formation of young red blood cells either directly or indirectly. Examination of the blood-count chart shows that the blood platelets were increased over the former figure after the removal of the spleen. There was a temporary reduction of the bleeding time. Bleeding from the gums ceased immediately after the operation. The total number of leukocytes was increased. This is usual after splenectomy. For a time the patient appeared to be improved clinically.

Transfusion of whole blood in our case appeared to be a useless

measure to control bleeding. It was of value in temporarily raising the content of red blood cells and hemoglobin in the circulation.

Operation was approached in the case of the patient here recorded with a certain degree of confidence, our feeling being that if the patient survived the operative procedure we might expect a cessation of her hemorrhagic symptoms. We were disappointed. The patient made a good recovery from a surgical viewpoint after the removal of the spleen, and evidence of stimulation of the functions of the blood-forming organs was evident after operation, but this was not sufficient for recovery.

We are aware of the fact that the final diagnosis in this case is somewhat problematical and that some may be inclined to consider it acute myelogenous leukemia with purpuric features. We have no desire to be dogmatic in our diagnosis. The bulk of the evidence appears to us to place the case as one of primary purpura hemorrhagica with stimulation myelocytosis. But we are quite willing to recognize that we may have the clinical entity, hemorrhagic purpura, merging in various degrees into the equally poorly limited field of leukemia.

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## DISCUSSION

Dr. George P. Müller: I have had no personal experience with splenectomy for this disease. There is no reason why it should not be tried, and even offer an advance in treatment, because our experience with certain other diseases shows that splenectomy is followed by good results. In hemolytic icterus and in the early stages of Banti's disease results have been excellent. In that form of pernicious anemia commonly called the "hemolytic," splenectomy combined with blood transfusion has given a number of improvements and a few remarkable cures. Lately, splenectomy has been advocated for leukemia, especially when there has been preliminary radiation of the spleen. The usual indications have been in those cases where the spleen apparently is destroying the red blood corpuscles, and in other cases, as in cirrhosis of the liver, where it is desired to reduce the blood load carried to the liver. As I understand it, splenectomy in purpura hemorrhagica is urged as a means of checking the destruction of blood platelets. It has been suggested that the operation is in the nature of a "shock" to the organism, and that similar results are obtained by the injection of various proteids, such as milk. Several years ago I performed a blood transfusion on a patient with pernicious anemia. The wrong donor evidently was used. Marked reactions of hemolysis and agglutination appeared and the patient nearly died. During forty-eight hours he only voided a few ounces of bloody urine, he developed a curious scarlatiniform rash. He recovered, showed a very marked improvement and remained well for about nine months, when he relapsed and in spite of several transfusions he died. I understand that there are about 70 cases

on record in which splenectomy has been done for this disease, with a fair percentage of apparent cures, a large percentage of improvement and in the chronic group a low mortality. On the other hand, in the acute group the mortality is prohibitive. I do not know whether or not Drs. Mitchell and Farley consider theirs as an acute or chronic case. Recently in the University Hospital, Drs. Fitz-Hugh, Prendergast and Pancoast have somewhat changed an older method in which radiation over the spleen was given in stimulant doses. They work in reversal and give a dose which has a destructive action on the spleen. Dr. Fitz-Hugh himself is here and will be glad to speak of this work. I do not think that anyone can foretell whether or not this operation is worth while until sufficient cases have accumulated.

Dr. Edward B. Krumbhaar: When the wave of splenectomy for pernicious anemia almost overwhelmed us, some ten years ago, undoubtedly many spleens were removed which should not have been, and now I feel that the wave has receded too far and more spleens should be taken out for pernicious anemia than is now the custom. It seems possible that this cycle may be repeated with purpura hemorrhagica, and certainly it would be a mistake to remove the spleens of all such cases. Dr. Müller has called attention to the different results in the acute and chronic forms, and I think this should always be emphasized and the splenectomized cases followed over long periods. In regard to Dr. Farley's case, which he was good enough to discuss with me a few months ago, I feel that he has been unduly hard upon himself. It should be noted that immediately after splenectomy the case behaved in the proper manner: the platelet count rose, the blood picture improved, the bleeding ceased and the patient was generally much improved. Then she "went bad," and here I would be inclined to emphasize the presence of a fecal organism in the blood stream (Bacillus fecalis alkaligenes). This with the partial high obstruction found at autopsy (with its well-known power of producing highly toxic substances) makes it possible—nay even probable—that this accident resulting from an anatomical defect was chiefly responsible for the patient's death. Another example of where the operation was successful, but the patient died.

Dr. Walter E. Lee: In answer to Dr. Krumbhaar's suggestion that the immediate cause of death in this patient was a blood-stream infection with an intestinal organism which resulted from intestinal obstruction, I feel it is only fair to add to Dr. Farley's notes that, instead of having clinical symptoms of obstruction, the patient had an uncontrollable diarrhea for the ten days preceding her death. Clinically this was the problem which was baffling the surgeon. It is true that she had this congenital hernia that Dr. Paul found at postmortem, but she never gave any history of obstructive symptoms from it before she came to the hospital and certainly had no symptoms of obstruction while under our care.

Dr. Thomas Fitz-Hugh, Jr.: I would simply like to mention a few points about the *x*-ray treatment Dr. Müller and Dr. Farley referred to.

We have been struck with the possibilities of combining the two main methods of treatment that have been recommended for purpura hemorrhagica, namely, protein shock and very massive doses, destroying the spleen with $x$-ray. The $x$-ray produces some sort of reaction that to my mind is a protein reaction. The spleen can be destroyed with the $x$-ray without destroying the patient. We have treated very few cases by this method, but those we have treated have responded clinically in a way just as favorably as those following splenectomy by the surgeons, with the exception that the platelets do not rise to the tremendous level following $x$-ray that is noted temporarily following splenectomy. A review of the results of splenectomy in the individual case reports indicates that most of the patients, although strikingly improved for a time at least, relapse into the previous condition of thrombocytopenia. I do not believe splenectomy has had long enough trial, for some of these cases reported as greatly improved or cured may not remain so, because purpura hemorrhagica is a notoriously unpredictable disease.

Dr. Harold W. Jones: We have had experience with only 2 cases of purpura hemorrhagica.

The first patient was admitted with a very low hemoglobin and red blood cell count; blood platelets, 10,000; bleeding time, eighteen minutes. After three transfusions, the amounts varying from 400 to 800 cc., she was discharged because she refused the operation of splenectomy and she refused to stay in the hospital. Her hemoglobin was 84 per cent; red blood cells, about 4,000,000; blood platelets, 46,000; bleeding time, ten minutes. About three months later she returned to the hospital complaining of epistaxis. We were unable to get a donor for her, she refused operation again, but this time the hemorrhage from the mucous membranes became more profuse and she died in a very short time.

The second patient was admitted with the characteristic signs and symptoms. Hemoglobin, 10 per cent; red blood cells, less than 1,000,000; bleeding time, thirty minutes; blood platelets, 26,000. She received six transfusions. She also refused operation and was discharged from the hospital with hemoglobin about 80 per cent; red blood cells, 3,950,000; blood platelets, 88,000; bleeding time, twelve minutes. Two years had elapsed since her discharge and I sent a communication to her husband, expecting that his reply would be that she had died. Instead she came up and presented herself for examination. Her hemoglobin was 78 per cent; red blood cells, 3,600,000; blood platelets, 110,000; bleeding time, twenty-one minutes. She had been able to do her work and the only symptom of which she complains is that she bruises easily.

Both of these cases refused splenectomy, and I mention them to show what can be done by blood transfusion alone in certain of these patients. It seemed to me that the name, essential thrombocytopenia, is not a good one for this disease, because, although the platelets are greatly reduced, even when the patient is well and symptom-free, the blood platelets are still greatly reduced and sometimes do not return to normal for months. Then, too, splenectomy, although followed immediately by an initial increase in platelets, is later followed by the platelets dropping to their former low level.

# THE TREATMENT OF CARBUNCLES*

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AND

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As one looks through the textbooks and the surgical literature at the present time for the accepted treatment of carbuncles it is surprising to see the lack of uniformity of the various authorities. Poulticing, *x*-ray, the injection of carbolic acid, strapping with adhesive plaster, are all advocated as conservative measures, while the total excision of the infected tissues with the cautery knife or the scalpel is advocated in practically all of the more recent textbooks.

Such a lack of uniformity in therapeutic measures usually indicates that none of the treatments recommended is entirely satisfactory. (This is particularly true of surgical procedures.)

Definition. Da Costa defines a carbuncle as a circumscribed infectious inflammation of the deeper layers of the true skin and of the subcutaneous tissues, with a fibrinous exudation and multiple foci of necrosis and gangrene frequently developing in the tissues adjacent to each necrotic plug. Stewart tersely describes carbuncles as boils containing multiple cores.

Etiology. A study of a group of over 150 cases, which began with our experimental work in the comparative values of antiseptics, has emphasized the necessity of understanding the etiological factors involved in this lesion in order to properly treat it.

Carbuncles are found most frequently on the nape of the neck, the back between the scapulæ, the buttocks and sometimes on the face and lips. In all of these areas the skin is thick and tough, and is bound to the underlying fascia by strong fibrous bands or septa in such a way as to form a series of intercommunicating cavities

* Read May 6, 1925.

containing fat, hair follicles and glands, and bounded above and below by tough skin and fascia. On account of these fibrous septa and the unyielding skin and fasciæ, the inflammatory exudate which occurs in response to pyogenic infection is confined and produces great tension in the involved area. The blood supply of the infected area is diminished by this pressure, and in consequence considerable portions of tissue are likely to die and form a slough. The pointing of the abscess cavities in carbuncles toward the surface and their rupture do not occur until late, owing to the thick, unyielding character of the skin. But there is an easy means of extension and relief of the pressure or tension in a lateral direction, through and among the septa of fibrous tissue, so that the adjacent fat columns very early become infected from the primary focus with which they communicate. In the secondary foci the process is repeated, namely, increase of tension, suppuration, early necrosis and further lateral spread, combined with the difficult access to the surface of the skin. In consequence, when the central fat columns have ruptured or discharged their contents of pus and necrotic tissue on the surface, the tension is not relieved in the spaces and pockets adjacent to them, and therefore the process continues to spread at the periphery.

The original infection probably takes place through an abrasion or a cut; it may rarely be due to conveyance by the blood or lymph streams. The causative organism is almost invariably the Staphylococcus pyogenes aureus, as in other skin infections. It is important to remember that there is no fundamental difference between a boil and a carbuncle, but the difference is due solely to anatomical and mechanical differences in the areas of tissue involved. A carbuncle is a multiple boil—a boil, if you will, with a college education.

Carbuncles are particularly apt to be found in those who are debilitated from other causes, for example, old age, diabetes, Bright's disease and in those recuperating from exhausting diseases. The appearance of a carbuncle should always be an indication to examine the urine for sugar and albumin.

Symptoms. The earliest *local symptoms* resemble those of a boil, but from the start the pain is usually more severe. The inflammatory area begins as a papule with an indurated base. It rapidly enlarges, is hot, dark red, tender, painful and swollen, often brawny on palpation, and is not freely movable on the underlying parts.

In a few days many pustules appear, and enlarged vesicles filled with bloody serum may form. In some cases, about the tenth day, the pustules may rupture and discharge freely, and the case slowly progress toward cure; but usually the carbuncle continues to spread at the periphery while the central pustules are discharging more or less freely. In such cases the deeper tissues are filled with pus, which is being incompletely discharged through the many small openings, each of which is partially blocked by a plug of dead tissue. Large masses of skin and subcutaneous tissues are destroyed; even the whole carbuncular area may become gangrenous. A sudden and practically complete cessation of pain points toward this complication.

The *general symptoms* begin usually with a chill and are almost always profound, especially in those frequent cases where the patient is already debilitated from other causes. Apathy and even coma are frequently seen, while on the other hand delirium is by no means rare. The temperature is of the septic type, and usually high, but may be subnormal. There is a high leukocytosis, as a rule, with an excess of polymorphonuclears, and absence of leukocytosis indicates either overwhelming infection or lack of resistance on the part of the patient. In exceptional cases, in which the disease is mild or the resisting powers unusually good, the constitutional effects may be very slight.

Prognosis. In the ordinary case the prognosis is good. A carbuncle remains acute for about three weeks, and healing requires at least another month. The most dangerous site of the lesion is on the face; over 50 per cent of those on the upper lip are fatal, due to a spreading septic thrombosis from the facial to the ophthalmic vein, which communicates with the cavernous sinus. Death may be caused by profound septicemia, pyemia, hemorrhage, septic thrombosis of the cerebral sinuses, or, especially in diabetes, by acidosis or coma.

Diagnosis. The diagnosis of carbuncle is made by noting the profound constitutional involvement and the multiple foci of necrosis on an inflammatory base, with rather rapid lateral extension. Although the diagnosis is usually easily made by inspection, still there are certain conditions which must at times be differentiated:

1. Boils are conical and have but one opening. They are associated with little or no constitutional involvement.

2. Gummata are painless, with but little inflammatory reaction. The edges are sharp and undermined. Their discharge is glairy and the slough looks like wet leather.

3. Anthrax is characterized by a black slough surrounded by a ring of vesicles. There is usually very marked edema of the surrounding tissues and swelling of the related lymph glands. There is little pain, though the constitutional reaction is often profound. There is no pus formation. The bacillus anthracis can be demonstrated in the vesicles surrounding the central slough.

4. Actinomycosis is a chronic infection; this alone is sufficient to distinguish it from carbuncle, which it somewhat resembles clinically. There is a multiplicity of sinuses in an enlarged and swollen base; but the discharge is a thin serous fluid, not pus, containing the pathognomonic sulphur granules, which microscopically consist of groups of the club-shaped fruiting bodies of the fungus.

Treatment. There are two indications in the treatment of all pyogenic infections—the relief of tension and the removal of dead tissue. A consideration of the anatomy and of the mechanical factors involved in carbuncular infections shows that a number of simple incisions into a carbuncle is ineffective in meeting either of the indications, except along the plane of the incisions themselves. Elsewhere the tension is not relieved, nor is the dead tissue removed. This will be made clear if we compare the carbuncular area to a piece of honeycomb, which it much resembles. The incisions into a honeycomb, even if crucial or multiple, open only those cells which are directly in the path of the knife. If, however, we make incisions in a plane at right angles to the crucial incisions, parallel to the surface, it is evident that all the cells will be freely opened.

After relief of tension has been obtained, the subsequent treatment of the infection consists in the surgical sterilization of the wound. This differs in no way from the principles of chemical sterilization which are applied in the treatment of any other form of suppuration. In other words, after we have relieved or removed the mechanical factors which make carbuncles instead of boils, we have the infection behaving exactly as a boil.

In the treatment of carbuncles as practised at the Pennsylvania Hospital, a crucial incision is made, extending well beyond the indurated area in all directions, thus dividing the involved area into four sectors. Each flap so formed is undercut, with an incision parallel to the skin and about midway between the skin and the deep fascia. This undercutting incision extends beyond the periphery of the indurated area and should be made with a sharp knife. Its purpose is to open freely all the infected columnæ

Fig. 1.—Carbuncle in a man aged seventy-two years. Duration twelve days.

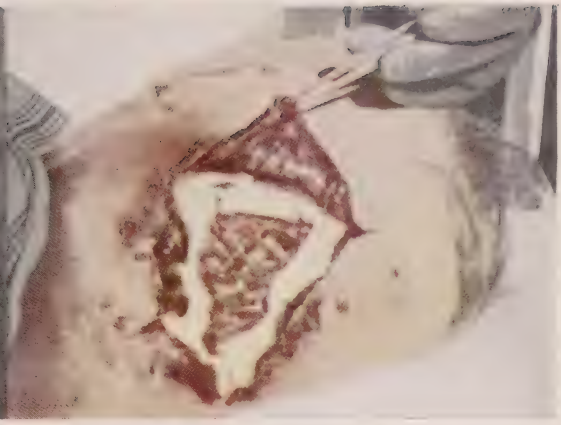
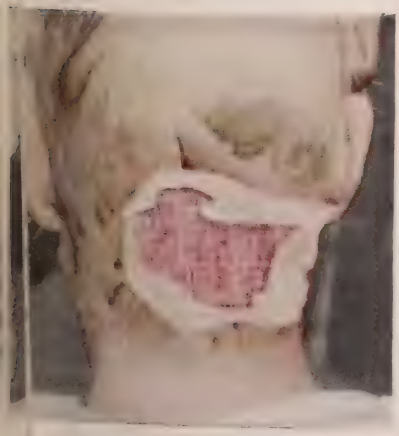


Fig. 2.—Crucial incisions, undercutting of flaps and packing of the wound with gauze saturated with a 5-per cent solution of dichloramine-T. Operation on the twelfth day.

Fig. 3.—Condition of wound when dressed four days after operation.

Fig. 4.—Condition of wound nine days after operation.



5.—Wide-meshed, paraffined gauze applied to granulating surfaces.

Fig. 6.—Condition of wound twenty-one days after operation.

Fig. 7.—Carbuncle of ten days' duration.

Fig. 8.—Crucial incision on the tenth day. Condition of wound on the thirteenth day and just before the secondary suture.

Fig. 9.—Condition of wo ten days after crucial inci and seven days after ondary suture.

adiposæ in the involved area, relieving the tension in each of them and allowing a free discharge of the pus. It acts as a similar incision does in tapping a honeycomb before the extraction of the contained honey.

After each flap is undercut it is elevated as one would the flap of an envelope, and pads of gauze soaked in some germicide, preferably of the chlorine group, are packed under them to prevent the flaps from collapsing into the wound. After twenty-four to forty-eight hours the gauze packs will be found loosened by the proteolytic effect of the exudate, and they are then removed. Systematic Dakinization of the wound is then practised. Under this treatment all the dead tissue and slough is removed within a few days—six to seven at the most. When this has been accomplished the skin flaps are replaced on the wound in their normal relations, and are allowed to become adherent to the underlying granulating tissues. In many instances time can be saved by the practice of secondary suture, or adhesive straps can be successfully used to hold the flaps in place. Primary union of the flaps so returned into place is the rule, except for the tip of each flap, where the skin has usually sloughed before the patient presents himself for treatment.

The end-result of this plan of treatment is a crucial linear scar which is wider at the crossing of the two incisions. This result is obtained, in the average case, in from three to four weeks from the time the treatment is instituted.

Other Methods. Other treatments have been more or less widely advocated. Strapping with adhesive plaster, poulticing and the multiple injection of carbolic acid are only mentioned to be condemned. They are painful, unsurgical, carry a very definite risk of pyemia and, worst of all, do not meet the surgical indications. The most these methods can do is to hasten the onset of gangrene of the whole area and its separation from the body as a slough.

*X*-ray treatments are sometimes successful in relieving the pain, but seem to have no other effect. We are not convinced that the advocates of this method have shown any diminution of the time of disability nor any reduction in the number of complications over untreated carbuncles.

Linear or crucial incisions do not fully meet the indications, as explained above, and such treatment is inefficient. Complete excision of the diseased area, of course, removes the whole carbuncle, but at the expense of total and permanent loss of a considerable

amount of viable tissue. This operation is followed by prolonged disability, often requires a secondary skin grafting or plastic operation for closure, and results in an extensive and unsightly scar which in itself has capacities for harm. Though undeniably efficient, it strikes one as unnecessarily heroic and destructive, and is no more to be recommended than the equally destructive process mentioned by Charles Lamb in his "Essay on Roast Pig." In this essay, it will be remembered that Lamb described the inhabitants of some hypothetical foreign country as in the habit of burning down the pigstye with its contained pigs whenever they felt inclined to eat roast pork.

Conclusions. In conclusion we feel that:

1. Carbuncles differ from other forms of suppuration in the subcutaneous tissues because of the anatomical and mechanical factors present in the region in which they occur, namely, a thick, tough true skin connected with the underlying fascia by strong vertical, fibrous septa. These factors not only delay the breaking of the original focus through the skin, but also force it to spread laterally and become pocketed in the honeycomb-like area.

2. The tension is perfectly relieved in all these pockets of infection when, in addition to the usual crucial incisions, incisions are made through each section parallel to the skin surface, which opens all the diseased fat columns. When this has been done, each area of infection acts like a separate boil and is able to drain freely onto the surface.

3. The simple crucial incision is not efficient; excision *in toto* is unnecessarily destructive and prolongs the time of disability.

4. Certain other treatments for carbuncles which have been advocated are discussed and reasons given for their condemnation.

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## DISCUSSION

Dr. Edward Martin: The discussion of this paper is something in the line of complete accord with its teachings. But, first, I would ask Dr. Lee—the high priest of gentleness, swiftness and efficiency in surgical dressing, not only the preacher, but the practitioner thereof, a believer in light and air for his wounds and in nontraumatizing and painless dressing—whether he does not sometimes see the necessity of using for packing beneath paraffin gauze mesh, some material which goes in easily, comes out easily and provides adequately for drainage? Perhaps as many crimes

have been committed through gauze improperly used as through the agency of any other thing a surgeon employs. I speak of this because I know it is his practice, but he has not made it distinctly clear. All painful dressings and all bleeding dressings are bad dressings. Gauze packing is usually painful when placed in the wound and causes bleeding when it is taken out. Moreover, it plugs as often as it drains.

In regard to the starting of carbuncles, they occur mostly in males and are seated on the back of the neck. They usually begin as an infected hair follicle. The rubbing of the collar causes some discomfort, but not enough to induce the wearer to discard this source of repeated slight trauma. Incident to this slight trauma, this inflamed follicle becomes a boil. Even then the collar may not be removed, though various home remedies are applied. Shortly the slight but frequently repeated trauma of the collar is supplemented by the powerful pressure of a friendly thumb. The boil becomes a carbuncle. Carbuncle can be prevented by pulling the hair at the root of which is a beginning inflammation, the application of dilute alcohol, which seems to be turned into formaldehyde in the skin, and protection against the repeated light trauma of a rubbing garment. If the infected follicle has formed a boil, it should be opened with a cataract knife sharpened to the degree that would satisfy the eye-man. After such opening, protection from trauma and the lightest form of fixed dressing usually insure against deep and wide extension of the infection.

In regard to infections of the upper lip: I do not know that they should be rightly called carbuncles, they are really a form of rapidly spreading cellulitis. I ask Dr. Lee whether he would, in such cases, turn up that thin skin in the hope of reaching an infection which seems to involve the entire thickness of the lip and has formed no foci of suppuration which possibly can be drained?

Dr. S. W. Moorhead: I want to speak in regard to the time for the application of treatment. I think that frequently our experience is that when a man has had a carbuncle very often he will recognize the nature of such a recurrent inflammation when it first starts. In such a case in my own experience I found that if, when the inflammation started, without waiting until slough appeared at the surface, a circumferential injection of novocain were made and deep incision with undercutting were performed the whole thing would clean up in about ten days.

Dr. Lee (closing): In answer to Dr. Martin's first question, I would say that the impregnation of gauze dressings with paraffin or vaseline before they are placed on wounds is not only ideal but it is entirely practicable. Undoubtedly, the results are better when the raw surfaces of wounds are protected in this way from the adherence of and consequent painful removal of dry gauze dressings. You may recall in one of the slides that the granulating surface of the carbuncle was covered by a wide-mesh paraffine gauze dressing, this with the double object of preventing adherence to the wound and permitting free drainage from the granulating surface.

With the carbuncles of the upper lip, undoubtedly, the pathology is

different from carbuncles in other parts of the body. The lesion is more diffuse and not as circumscribed and is more like a cellulitis, yet in the few that we have encountered we have opened them radically, not using the crucial incision here described because of the resulting deformities, but have made parallel incisions, placing them as near as possible in the creases of the face, and then have undercut these parallel incisions, thus dividing the vertical fibrous septa in the same way as we have described with the crucial incision.

In answer to the question as to the early treatment of furuncles and boils, and particularly as to the time such treatment should be instituted, we feel very definitely that the early and adequate treatment of these infections will usually prevent their developing into carbuncles. By this we mean that if it is possible to find the infected hair follicle, which is usually the focus of infection, and remove the hair, the adequate drainage thus provided may often arrest the progress of the infection. If, however, the focus cannot be so accurately located, one can always relieve the tension in these early infections by a free incision and by the relief of tension thus restore the blood supply which is so necessary for the full effect of the vital resistance of the tissues to bacterial growth. The vital resistance of human tissues to bacterial growth depends largely upon the blood supply to the part. The blood supply insures the bringing to the part of the leukocytes with their phagocytic power, together with the antitoxins and the bacteriolysins of the blood serum. This, of course, is expressed by the well-known phenomenon of inflammation. If the virulence of the bacteria be greater than that of the forces of vital resistance, the blood cells and the tissue cells will be destroyed and the result will be dead tissue. With this accumulation of dead tissue and vascular exudate in the perivascular tissues there will, of course, be an increase in the tension, which frequently reaches such a point as to interfere with and often stop the necessary supply of blood to the part. When this point is reached a vicious circle is established, because with the decreased supply of blood the vital resisting forces are handicapped and in addition the dead tissue provides ideal culture material for the growth of the bacteria. The link in this vicious circle of bacterial injury, increased blood supply and with its accompanying phenomenon of inflammation, increased perivascular tension, death of vascular and perivascular tissues from bacterial poisons and loss of blood supply, and resulting in a further increase of perivascular tension, is this factor of tension. If this abnormal tension can be relieved and the blood supply restored we will again be able to obtain the maximum effect of the vital resistance of the individual. Therefore, the indication at the beginning of all accessible infections is the complete removal of the focus, if possible, and if this is not possible, a wide incision which will not only relieve the tension that may exist as the result of the inflammatory exudate, but prevent development of any further tension that will embarrass and probably prevent the necessary blood supply to the part.

# EXPERIMENTS BEARING ON THE INFLUENCE OF FOCAL INFECTION AND THE PATHOLOGY OF ARTHRITIS *

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AND

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It is the purpose of this communication to present experimental data which bear upon the nature of the influence of focal infection and the pathology of arthritis. Some phases of the work also throw light on carbohydrate metabolism and this aspect has been elsewhere discussed.[1] In order to make plain the significance of the experiments and the reasoning which has led up to them, a brief summary of some previous work will be necessary. This summary, together with new data, will be taken up in the following order:

1. The sugar tolerance in arthritis.
2. The blood gases in arthritis.
3. Absorption from the gastrointestinal tract in arthritis.
4. The influence of the circulation on the sugar tolerance in arthritis.

In view of the interdependence of the several parts of the present studies a certain amount of repetition will be unavoidable.

The Sugar Tolerance in Arthritis. In the course of a study of chronic arthritis in the army it was demonstrated by Pemberton and Foster that a lowered sugar tolerance accompanies this disease in over 60 per cent of all cases.[2] The present writers have found a low sugar tolerance in 53 per cent of 77 arthritics in civil life. Comparable results have been reported by Holsti,[20] Fletcher,[14] Warfield[21] and Hench.[22]

Observations on a long series of cases showed that this lowered

* Read June 3, 1925.

tolerance is more or less proportional to the severity of the arthritis. It was also shown that as arthritics improve, irrespective of the measures accomplishing this, this lowered tolerance returns or tends to return to normal. It was also shown, however, that this return to normal is most abrupt after the removal of a causative focus of infection. This point is well illustrated in the following example of a soldier, aged nineteen years, with acute arthritis of one hip and greatly diseased tonsils. On February 27, after feeding 100 gm. of glucose, the sugar reached 190 mg. per cent. Two weeks later, on March 14, his tonsils were removed and he made a prompt recovery from the arthritis. On March 28, two weeks after his tonsillectomy, study of his sugar tolerance gave a normal curve. As a corollary to this can be cited another case, that of a large, robust soldier, studied as a normal control, in whom a normal sugar tolerance was obtained, the blood sugar not rising above 127 mg. per cent. Fourteen days later, however, he developed an acute frontal sinusitis, and three days after the onset of this a lowered sugar tolerance was obtained, the blood sugar reaching 185 mg. per cent with a slight glycosuria.

As remarked above, a lowered sugar tolerance in arthritis may return to or toward normal following the institution of other successful measures of therapy, such, for example, as the use of nonspecific protein or the application of a lowered caloric intake.[2]

It is clear, therefore, that a lowered sugar tolerance stands in close relation to the phenomena of arthritis on the one hand and the influence of frank focal infection upon the other.

A lowered sugar tolerance, however, is by no means specific for arthritis. It was observed by Hamman and Hirschman[3] to stand in some relation to certain thyroid disturbances and it has been observed to accompany furunculosis.[4] It has been alleged to accompany certain other nondiabetic conditions, but the evidence as to this is not final, and it seems probable at the present writing that, in some of these at least, it is a function of an unrecognized inflammatory process or focal infection. This point is brought out in a series of miscellaneous causes studied by Pemberton and Foster.[2]

Attention has been elsewhere[1] called to the fact that the lowered sugar tolerance of arthritis differs from that seen in diabetes in that there is no failure of combustion of glucose[5] and that the characteristic effect of insulin is evidenced by a fall in blood phosphorus.[1] Up to a certain renal threshold[2] there is no glycosuria, and observa-

tion of arthritics over a long series of years shows that they develop nothing of the diabetic syndrome. In fact, it has been shown by one of the present writers that the combination of arthritis and diabetes is at least unusual[6] and severe coincident examples of each have not been encountered. It will be shown later that the low sugar tolerance here under discussion can arise by a different process.

Attention is here directed at considerable length to the mechanism of a lowered sugar tolerance because of the degree to which it parallels arthritis and because of the paucity of data reflecting the dynamic pathology of this disease. It was believed that data elucidating this mechanism would contribute importantly toward an understanding of arthritis.

The Blood Gases in Arthritis. Attention has been called previously[6] to the fact that measures which increase the local or systemic bloodflow or the systemic metabolism tend to have a favorable influence upon the rheumatoid syndrome. Examples of this are to be seen in the effects of massage, exercise and the application of external heat.[7] Studies were therefore carried out upon the respiratory functions of the blood with the aim of seeing whether these are at fault in arthritis. In a series of such studies by Pemberton, Hendrix and Crouter[8] no disturbance of the dissociation curves of the blood for oxygen or carbon dioxide could be detected, but it was observed that during the conduction of a test revealing a lowered sugar tolerance there takes place in most cases a rise in the percentage saturation of that blood with oxygen. That is to say, the ratio of the oxygen content to the oxygen capacity increases, which means that more oxygen is left unutilized. It was further observed that there existed between groups of normals and groups of arthritics studied a small difference in the percentage saturation of the peripheral venous blood with oxygen. This series has since been extended and now includes 132 arthritics and 15 normals. The average percentage oxygen saturation of hemoglobin for the arthritics is 56 and for the normals 43. The figures for normals are in general consonance with those obtained by Cullen and Robinson.[9] They obtained an average of 53 per cent upon 23 supposedly normal students who had, however, partaken of a moderate breakfast in contrast to the normals studied by us who were fasting. Our figures and those of Cullen and Robinson are lower than those of some other workers.[10, 11]

This difference is presumably due to a number of factors not wholly understood, but in the present connection we are concerned only with a comparison of the arthritic and normal bloods obtained under identical conditions. The difference between the average for the groups of normals and arthritics is small and will not bear much emphasis, but on analysing the figures for arthritics, from which the average for that group was made up, it appears that some cases gave higher figures than were ever shown by normal individuals. Thus, the range for normals is from 27 to 67 per cent and for arthritics from 25 to 95 per cent. There is, therefore, limited but definite evidence that the peripheral venous blood in arthritics may show a higher percentage saturation with oxygen than occurs in health under similar conditions. Some explanation of this is afforded by the following:

In the course of study of the influence of various measures having benefit toward the rheumatoid syndrome, attention was directed to the application of external heat. It was observed, among other findings, by Pemberton, Hendrix and Crouter[8] that the percentage oxygen saturation of the peripheral blood tends to rise as the result of the subjection of an individual to an electric bake applied in the usual therapeutic manner. This rise in the oxygen saturation is presumably due to the acceleration in the circulation which occurs, and is in keeping with the statement by Wells[12] that blood from a hyperemic area contains more oxygen and less $CO_2$ than normally.

These several observations suggest that in the arthritic there is a change in the circulatory conditions or rate such that the tissues do not extract from the blood as it passes through them the usual amount of available oxygen. In connection with the bloodflow in arthritis it is to be noted that analysis of the beneficial effects of external heat, massage and exercise upon the rheumatic syndrome[7] shows that the first and last of these measures produce opposite effects upon the acid base equilibrium of the blood and that the favorable influences of all three measures are apparently due chiefly to their effect on the circulation.

Absorption from the Gastrointestinal Tract in Arthritis. It has been further observed by one of the present writers[13] that in a considerable percentage of arthritics, particularly of the so-called proliferative type, undoubted benefit may accrue from the application of a reduced caloric intake. This observation has been corroborated by Fletcher,[14] in two series of 50 and 100 cases, respec-

tively, by Cecil and Archer[23] and by others. It seemed possible therefore, in view of the evidence suggesting an increased circulatory rate in arthritics, that in arthritis absorption from the intestinal tract and stomach might take place too rapidly and that the influence of a lowered dietary could be explained by avoidance of an abrupt or undue absorption. It seemed also possible, for the same reason, that the lowered glucose tolerance in arthritis might be referable to an unduly rapid absorption of glucose. It was, therefore, determined to test this by feeding urea and potassium iodide coincidentally with the glucose in the conduction of a test for lowered sugar tolerance. If the difference between a normal and lowered sugar tolerance is largely a difference in the rate of absorption of sugar from the gut, corresponding differences in the rise of nonprotein nitrogen in the blood and in the rate of excretion of nitrogen and iodide might be expected when urea and potassium iodide are given with the sugar. Urea and potassium iodide are diffusible substances, presumably readily absorbed from the intestinal tract. Mendel and Baumann,[15] found that potassium iodide is absorbed from the mammalian stomach. In the present studies nonprotein nitrogen of the blood and total urinary nitrogen were determined by Folin's methods.[16] Iodides were determined in the urine by oxidizing the iodide to iodine with nitrous acid, extracting the iodine with chloroform and, after washing the chloroform free of $HNO_2$, titrating the iodine present with $\frac{N}{100}$ sodium thiosulphate.[17] The appended tables show, however, that the nonprotein nitrogen of the blood rose no higher in cases with a low sugar tolerance, and therefore a high concentration of sugar in the blood, than it did in cases showing a normal sugar tolerance and therefore a low glucose concentration. Similarly the excretion of iodine and total nitrogen in the urine showed no increase in the urine per thirty-minute periods in the cases of low sugar tolerance as compared with the cases of normal tolerance. There is therefore no suggestion that an increased rate of absorption accounts for the variety of low sugar tolerance under discussion. These observations left the matter open to some other explanation. As an alternative, it seemed possible that the mechanism producing a high percentage saturation of oxygen during the conduction of a test revealing a lowered sugar tolerance was referable, not to an increased rate of circulation, but, to a failure of the blood adequately to reach certain areas or tissues of the body. The

effect of this would be, equally, to leave unutilized some of the available constituents of the blood. This explanation would also account for the higher percentage saturation observed in some fasting arthritics.

TABLE I.—ABSORPTION FROM THE ALIMENTARY TRACT IN ARTHRITIS FOLLOWING INGESTION OF GLUCOSE, UREA AND POTASSIUM IODIDE.

| Subject. | Blood analysis. | | | | Urine analysis. | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Date (1924). | Time (min.). | Blood sugar mg. per 100 cc. | Non-protein nitrogen mg. per 100 cc. | Time (min.). | Volume cc. per half hour. | Iodine mg. per half hour. | Total nitrogen mg. per half hour. | Sugar (gm.). |
| Seg. | 12–9 | 0 | 86 | 28 | 35 | .. | 16 | .. | 0 |
| | .. | 30 | 143 | 33 | 70 | 150 | 10 | 241 | 0 |
| | .. | 60 | 164 | 39 | 140 | 10 | 13 | 96 | 0 |
| Mur. | 12–15 | 0 | 90 | 26 | 25 | 25 | 0 | .. | 0 |
| | .. | 30 | 167 | 31 | 55 | 25 | 7 | .. | 0 |
| | .. | 75 | 139 | 32 | | | | | |
| | .. | 95 | 137 | 38 | 105 | 24 | 10 | .. | 0 |
| How.* | 12–18 | 0 | 81 | 23 | 30 | 26 | 0 | .. | 0 |
| | .. | 35 | 125 | 25 | 75 | 38 | 9 | .. | 0 |
| | .. | 65 | 102 | 32 | 130 | 33 | 13 | .. | 0 |
| | (1925). | | | | | | | | |
| Dal. | 1–14 | 0 | 85 | 28 | 0 | .. | 0 | .. | 0 |
| | .. | 30 | 125 | 31 | 35 | 20 | 3 | .. | 0 |
| | .. | 75 | 110 | 36 | 90 | 55 | 10 | .. | 0 |
| | .. | .. | .. | .. | 170 | 60 | 13 | .. | 0 |
| Daug. | 1–19 | 0 | 95 | 34 | 40 | 30 | 1 | .. | 0 |
| | .. | 30 | 176 | 40 | 90 | 30 | 8 | 285 | 0 |
| | .. | 85 | 186 | 38 | 140 | 36 | 12 | 359 | 0 |
| Proc. | 1–20 | 0 | 78 | | | | | | |
| | .. | 30 | 128 | 33 | | | | | |
| | .. | 90 | 85 | 35 | 190 | 10 | 3 | .. | 0 |
| Hol. | 1–22 | 0 | 97 | 38 | 0 | 14 | 0 | 147 | 0 |
| | .. | 30 | 139 | 42 | 45 | 12 | 2 | 134 | 0 |
| | .. | 60 | 215 | 48 | 105 | 15 | 10 | 235 | 0 |
| Keen. | 1–31 | 0 | 95 | 39 | 0 | 8 | 0 | 123 | 0 |
| | .. | 40 | 179 | 40 | 45 | 23 | 2 | 194 | 0 |
| | .. | 85 | 166 | 42 | 90 | 30 | 7 | 333 | 0 |
| Fla. | 2–20 | 0 | 100 | 38 | 0 | 15 | 0 | 173 | 0 |
| | .. | 30 | 129 | 39 | 40 | 25 | 2 | 236 | 0 |
| | .. | 60 | 130 | 43 | 85 | 45 | 9 | 298 | 0 |

* Normal individual.

THE INFLUENCE OF THE CIRCULATION ON THE SUGAR TOLERANCE IN ARTHRITIS.† It was therefore determined, as an experimentum crucis, to reduce the bloodflow or interfere with it in some part or parts of the body, in such a way as to simulate a condition in which, for example, a large capillary area is closed and then to conduct a test of sugar tolerance in the usual manner. A positive result,

† Obligation should be expressed to Dr. E. G. Peirce for coöperative assistance in several phases of this work.

showing the induction of a lowered tolerance, would be obviously confirmatory of the above hypothesis. The method decided upon was to place normals and arthritics, whose sugar tolerance had been determined as essentially normal, in the recumbent position with the legs and one arm elevated at right angles to the body and then to carry out a test of sugar tolerance in the usual manner. In practice it was found useful for the subject to lie upon a bed whose head or foot touched a wall and to allow the elevated legs to rest against the wall for support, thus obviating any muscular or other effort. The elevated arm was supported by a pillow and by a loop of bandage, attached to a clothes tree, through which a finger could be hooked. This position was maintained throughout the experiment for one hour or one hour and a half. Shortly after raising the legs, evidences of inadequate circulation were apparent in the low surface temperature, quick collapsing pulse in the dorsalis pedis artery and, later, a gray cyanosis. In some cases cramps of the posterior tendons or muscles of the calf or thigh occurred. The blood under these circumstances doubtless reaches the periphery of the limbs concerned, in a somewhat explosive manner after the fashion of a Corrigan pulse since the column within the vessels during diastole lacks its usual support or *visa tergo*. By the same token, it would appear that the venous return is much expedited by gravity, the valves being designed to operate in the opposite direction, so that the tissues as a whole have a curtailed contact with the blood and less opportunity for the respiratory and other interchanges.

Experiments were carried out on 2 normals and 13 arthritics. The data show that in an important percentage of arthritics (60 per cent) who have had from the outset, or have acquired, an essentially normal sugar tolerance, it is possible, by means of interfering with the bloodflow in three limbs, to induce a lowered sugar tolerance comparable to that seen in 60 per cent of arthritics at large. This low tolerance has been induced, so far, in the arthritics only and not in the normals. This fact may relate it to a possible exaggeration, by the position assumed, of a comparable, already existing state of affairs in the peripheral circulation, rather than merely to a disturbance of circulation created *de novo*. A striking feature of the charts is the slant of the curves which show, in most instances, that not only was the blood sugar higher in the experimental position at the end of an hour but it was still mounting when in the normal position it had already fallen.

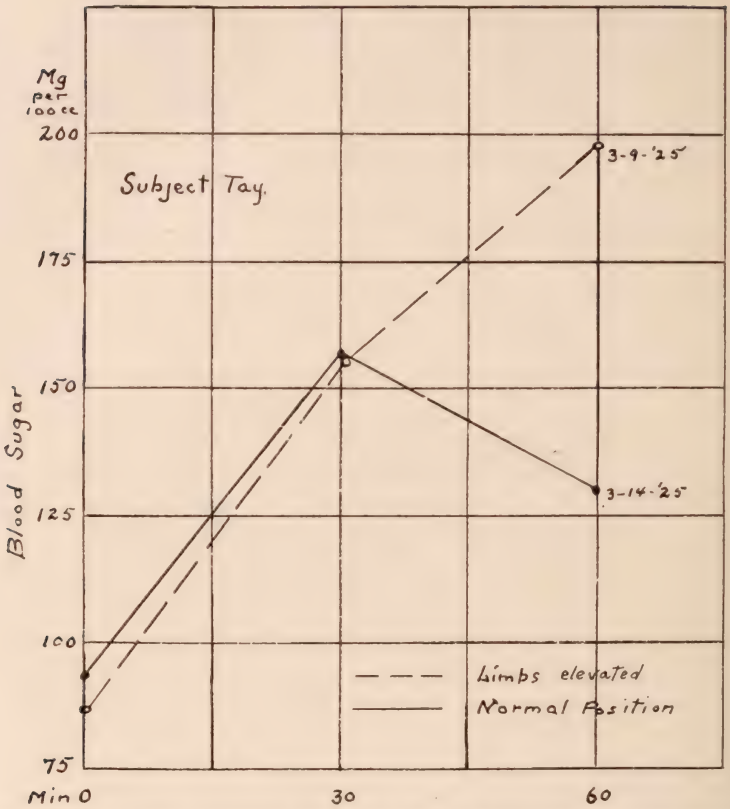


CHART 1.—The effect of postural interference with the circulation on sugar tolerance. (Subject, "Tay").

It will be noted by referring to Table III that a marked diuresis accompanied practically all cases in which the legs were elevated. A definite increase in alkalinity was observed to accompany the diuresis in most cases in keeping with the experience of others who have studied urinary volume and pH.[18, 19] This diuresis suggests an influence upon the kidneys and it is not inconceivable that the adrenals may be affected also in view of their close anatomical relation to the kidneys.

A comparable diuresis has been observed by Griffith and Hansell[24] as the result of extra-abdominal pressure.

The relation of these findings to carbohydrate metabolism has been discussed elsewhere.[1] Mention only will be made of the fact that observations on the blood sugar after assumption of the

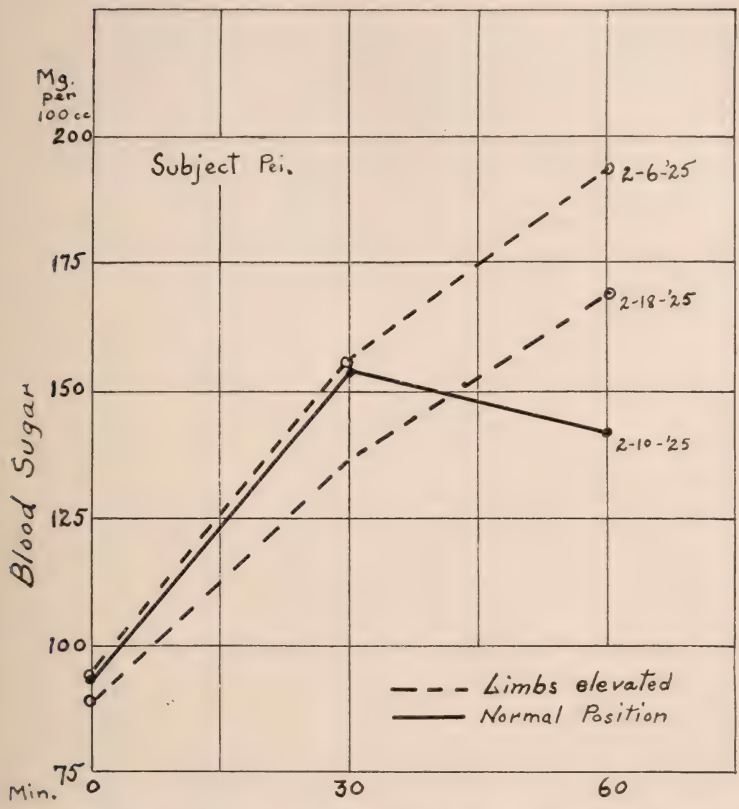


CHART 2.—The effect of postural interferencewith the circulation on sugar tolerance. (Subject, "Pei").

experimental posture, when uninfluenced by glucose feeding, show no increase in sugar. This indicates that the degree of "anemia" in the elevated limbs is not sufficient to cause asphyxia of the tissues and hence hyperglycemia from this cause. It also indicates that hyperemia of the adrenals is not an operative factor under fasting conditions following the experimental position.

The evidence therefore strongly indicates, that, whether or no any additional mechanism be concerned, denial to the muscular tissues of their usual degree of contact with the circulating blood, interferes with the withdrawal of glucose, so that when sugar is fed, a lowered tolerance results.

Preliminary announcement of work being conducted in this laboratory by Dr. E. G. Peirce is also made at this time.

TABLE II.—THE EFFECT OF CIRCULATORY CHANGES, RESULTING FROM ELEVATION OF THE LIMBS, ON THE SUGAR TOLERANCE OF ARTHRITICS

| Subject. | Seated. | | | Legs elevated. | | |
|---|---|---|---|---|---|---|
| | Date (1925). | Time (min.). | Blood sugar, mg. per 100 cc. | Date (1925). | Time (min.). | Blood sugar, mg. per 100 cc. |
| Pei. | 2–10 | 0 | 94 | 2–6 | 0 | 94 |
| | .. | 35 | 154 | .. | 30 | 155 |
| | .. | 65 | 142 | .. | 60 | 193 |
| | .. | .. | .. | 2–18 | 0 | 88 |
| | .. | .. | .. | .. | 30 | 137 |
| | .. | .. | .. | .. | 60 | 169 |
| Ca.* | 4–10/24 | 0 | 99 | 2–12 | 0 | 88 |
| | .. | 45 | 112 | .. | 30 | 119 |
| | .. | 90 | 109 | .. | 60 | 104 |
| Wh.* | .. | .. | .. | 2–13 | 0 | 86 |
| | .. | .. | .. | .. | 35 | 111 |
| | .. | .. | .. | .. | 75 | 84 |
| Sul. | 2–19 | 0 | 87 | 2–16 | 0 | 90 |
| | .. | 30 | 135 | .. | 30 | 131 |
| | .. | 60 | 132 | .. | 60 | 123 |
| Mur. | 2–20 | 0 | 81 | 2–17 | 0 | 90 |
| | .. | 30 | 157 | .. | 30 | 169 |
| | .. | 65 | 124 | .. | 60 | 197 |
| Ing. | 2–28 | 0 | 87 | 2–25 | 0 | 94 |
| | .. | 30 | 162 | .. | 35 | 164 |
| | .. | 60 | 177 | .. | 65 | 162 |
| Hei. | 3–19 | 0 | 88 | 3–3 | 0 | 87 |
| | .. | 30 | 137 | .. | 30 | 122 |
| | .. | 60 | 164 | .. | 60 | 148 |
| Shr. | 4–25 | 0 | 86 | 3–4 | 0 | 91 |
| | .. | 35 | 148 | .. | 30 | 144 |
| | .. | 65 | 182 | .. | 65 | 205 |
| Fra. | 3–10 | 0 | 95 | 3–4 | 0 | 88 |
| | .. | 30 | 108 | .. | 35 | 133 |
| | .. | 60 | 97 | .. | 65 | 162 |
| Bro. | 3–12 | 0 | 101 | 3–5 | 0 | 105 |
| | .. | 30 | 149 | .. | 30 | 161 |
| | .. | 60 | 153 | .. | 60 | 176 |
| Wy. | 3–13 | 0 | 104 | 3–6 | 0 | 94 |
| | .. | 55 | 168 | .. | 50 | 156 |
| | .. | 95 | 159 | .. | 85 | 161 |
| Tay. | 3–14 | 0 | 91 | 3–9 | 0 | 87 |
| | .. | 30 | 156 | .. | 30 | 155 |
| | .. | 60 | 130 | .. | 60 | 198 |
| Gif. | 3–16 | 0 | 92 | 3–11 | 0 | 86 |
| | .. | 32 | 150 | .. | 30 | 152 |
| | .. | 65 | 101 | .. | 60 | 155 |
| Owe. | .. | .. | .. | 2–24 | 0 | 87 |
| | .. | .. | .. | .. | 30 | 112 |
| | .. | .. | .. | .. | 60 | 89 |
| Vorh. | .. | .. | .. | 3–17 | 0 | 89 |
| | .. | .. | .. | .. | 30 | 121 |
| | .. | .. | .. | .. | 65 | 130 |

* Normal individual.

Dr. Peirce has compared the erythrocyte count in the first drop of blood shed, following lancing of the finger, with the count in the subsequent drops from the same incision.

The subject was required to remain quiet five minutes with the hand resting comfortably in a horizontal position on a table. An

incision, sufficiently vigorous to produce a free flow of blood was then made with a lancet. Great care was taken to avoid conditions that would necessitate any squeezing or milking of the finger. After the first drop was used for the count, at least four drops were wiped off and a second sample then taken. The best results were obtained early in the morning before the subject had indulged in much activity and at a time when there had been nothing to excite or cause apprehension to the subject. Absolute care and uniformity of technic and procedure were necessary in order to obtain consistent results.

TABLE III.—THE EFFECT OF ELEVATION OF THE LIMBS ON THE SECRETION OF URINE

| Subject. | Seated. | | | | | | Legs elevated. | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Date (1925). | Sample.* | Vol. cc. per hr. | Specific gravity. | pH. | Sugar (gm). | Date (1925). | Sample.* | Vol. cc. per hr. | Specific gravity | pH. | Sugar (gm.). |
| Pei. | .. | .. | .. | .. | .. | .. | 2–18 | 1 | 169 | .. | 6.4 | 0 |
| | .. | .. | .. | .. | .. | .. | .. | 2 | 324 | .. | 6.6 | 0 |
| Sul. | 2–19 | 1 | 70 | .. | 6.8 | 0 | 2–16 | 1 | 42 | .. | 6.0 | 0 |
| | .. | 2 | 146 | .. | 7.0 | 0 | .. | 2 | 275 | .. | 6.8 | 0 |
| Mur. | 2–20 | 1 | 51 | .. | 6.8 | 0 | 2–17 | 1 | 40 | .. | 5.2 | |
| | .. | 2 | 88 | .. | 6.8 | 0 | .. | 2 | 276 | .. | 6.6 | 0 |
| | .. | .. | .. | .. | .. | .. | 6–12† | 1 | 35 | 1.023 | 6.4 | |
| | .. | .. | .. | .. | .. | .. | .. | 2 | 100 | 1.013 | 7.2 | |
| Ing. | 2–28 | 1 | 72 | 1.021 | 7.2 | 0.0 | 2–25 | 1 | 51 | 1.020 | 7.8 | |
| | | 2 | 25 | 1.026 | 6.0 | 0 | | 2 | 224 | 1.010 | 7.2 | 0 |
| Hei. | 3–19 | 1 | 55 | 1.015 | 5.4 | 0 | 3.3 | 1 | 99 | 1.006 | 6.4 | 0 |
| | | 2 | 83 | 1.011 | 6.4 | 0 | | 2 | 168 | 1.005 | 6.4 | 0 |
| Shr. | 4–25 | 1 | 38 | 1.32 | 5.0 | 0 | 3–4 | 1 | 17 | .. | 5.0 | 0 |
| | | 2 | 142 | 1.015 | 5.4 | 0.86 | | 2 | 77 | .. | 6.0 | 1.0 |
| Fra. | 3–10 | 1 | 35 | 1.029 | 5.2 | 0 | 3–4 | 1 | 22 | 1.022 | 5.0 | 0 |
| | | 2 | 45 | 1.025 | 6.0 | 0 | | 2 | 238 | 1.006 | 5.2 | 0 |
| Bro. | 3–12 | 1 | 26 | 1.032 | 5.0 | 0 | 3.5 | 1 | 30 | .. | 5.2 | 0 |
| | | 2 | 27 | 1.030 | 5.2 | 0 | | 2 | 139 | 1.011 | 6.4 | 0 |
| Wy. | 3–13 | 1 | 51 | 1.016 | 6.2 | 0 | 3–6 | 1 | 54 | 1.017 | 6.0 | 0 |
| | | 2 | 178 | 1.007 | 6.6 | 0 | | 2 | 345 | 1.006 | 6.6 | 0 |
| Tay. | 3–14 | 1 | 33 | 1.025 | 5.4 | 0 | 3–9 | 1 | 35 | 1.021 | 5.0 | 0 |
| | | 2 | 244 | 1.006 | 6.8 | 0 | | 2 | 323 | 1.003 | 6.6 | tr. |
| Gif. | 3–16 | 1 | 24 | 1.023 | 5.0 | 0 | 3–11 | 1 | 20 | 1.026 | 6.5 | 0 |
| | .. | 2 | 33 | 1.024 | 5.2 | 0 | .. | 2 | 136 | 1.010 | 7.4 | 0 |
| | .. | .. | .. | .. | .. | .. | 6–9† | 1 | 7 | .. | 5.2 | |
| | .. | .. | .. | .. | .. | .. | .. | 2 | 20 | .. | 6.8 | |
| Ca.‡ | .. | .. | .. | .. | .. | .. | 2–12 | 1 | 34 | | | |
| | .. | .. | .. | .. | .. | .. | .. | 2 | 56 | .. | .. | 0 |
| Wh.‡ | .. | .. | .. | .. | .. | .. | 2–13 | 1 | 58 | .. | .. | 0 |
| | .. | .. | .. | .. | .. | .. | .. | 2 | 167 | .. | .. | 0 |
| Har. | .. | .. | .. | .. | .. | .. | 6–1† | 1 | 51 | 1.019 | 5.2 | |
| | .. | .. | .. | .. | .. | .. | .. | 2 | 216 | 1.006 | 6.8 | |

* Sample 1 was obtained before the experiment; sample 2 at the end of the experiment.
† No sugar taken.
‡ Normal individual.

It was found that differences exist in the red count of the first drop and the subsequent free-flowing drops when the blood is taken under the carefully controlled conditions described above.

It has been recognized by clinical microscopists that the first drop is not to be used for routine counts. In normal individuals the red count is usually higher by 200,000 to 400,000 in the first drop than in the later drops. In patients with arthritis, however, the situation is usually reversed and the first drop has a lower red cell content by 100,000 to 600,000.

These results are interpreted as indicating that in the finger of the arthritic there are relatively few open capillaries and the first drop of blood is diluted by tissue juice. Later drops represent more nearly the undiluted blood as it is pumped from the arterial system.

This work is being continued and extended and the present report is preliminary in character.

That circulatory changes contribute therefore to the pathology of arthritis and constitute part of the effects of focal infection, with both of which a lowered sugar tolerance is so closely associated, is thus clearly suggested. If these observations be correlated with the clinical benefits known to follow measures which improve the bloodflow in arthritis, this suggestion becomes even stronger.

SUMMARY. 1. In order that the significance of the present studies may be apparent a review is presented of the previous work and line of reasoning which have led to them. They are then discussed.

It has been shown that 60 per cent of all arthritics present a lowered sugar tolerance and that this tolerance returns toward or to normal after recovery from arthritis, whatever the therapy employed. It does so most abruptly, however, after removal of causative focal infection. As a corollary to this, the occurrence of an inflammatory process, such as sinusitis, may induce a lowered sugar tolerance in a previously healthy subject with a normal tolerance.

2. Studies of the blood gases during the conduction of a test revealing a low sugar tolerance, showed that the per cent oxygen saturation of the blood rises in a large majority of cases. The failure to relate this to chemical processes, implies that the blood fails to reach all tissues of the body or that the circulation is accelerated. In either event the result would be to leave some of the normal constituents unutilized. In this connection it has been shown in a series of arthritics and normals under identical conditions, that the average per cent oxygen saturation of the peripheral blood of the arthritics is higher in the ratio of 56 to 43. The range for the arthritics was 25 to 95; for the normals from 27 to 67.

3. In a considerable proportion of arthritics, particularly of the "proliferative" type, the application of a restricted caloric diet is of benefit. In view of the suggestions, above afforded, of a possibly increased rate of circulation in arthritis, the hypothesis was advanced that absorption from the gastrointestinal tract might in consequence be unduly rapid. The benefits of a reduced diet would then be referable to the avoidance of an undue, or unduly rapid, absorption and the occurrence of a low sugar tolerance would be referable to too rapid absorption. This hypothesis was then tested by feeding urea and potassium iodide, coincidentally with the sugar, to arthritics with normal and lowered sugar tolerance. The nonprotein nitrogen of the blood and the urinary iodide and nitrogen did not change commensurately with the blood-sugar, however. The results gave no support to the theory of an increased rate of absorption in arthritis and left, as one alternative, the theory that the blood inadequately reached some tissues. This failure to reach all tissues might result from closed capillary beds, and would, equally leave some of the blood constituents unutilized.

4. This hypothesis was therefore tested by interfering, through posture, with the bloodflow in the limbs of arthritics and normals and then conducting a glucose tolerance test. The results showed that in one-half of the cases studied it was possible to induce a lowered sugar tolerance in subjects presenting otherwise a normal sugar tolerance. In view of the close relationship of a lowered tolerance to arthritis and focal infection, this evidence approaches proof that a disturbance of the circulation, probably in the nature of closed capillary areas, constitutes an important part of the pathology of arthritis and the rheumatoid syndrome. If these findings be correlated with the well-recognized benefits accruing in arthritis from measures which improve the circulation, the evidence becomes stronger.

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## DISCUSSION

Dr. David Riesman: Arthritis is one of the most obscure and difficult subjects in medicine, as everyone knows who has attempted to study it. It ranks with the common cold as a condition upon which medical science, despite its wonderful progress, had made little impression. Perhaps the most promising contribution to the subject of arthritis is the theory of focal infection, for which the Chicago school deserves great credit. It might, however, be of interest to point out two historic facts that may not be generally known, namely, that Benjamin Rush, in a letter dated about 1803, referred to the possibility that diseased and carious teeth might cause general disorders, and that about one hundred or more years before him a great French surgeon, Jean Louis Petit, made a somewhat similar observation. As for myself, I am a firm believer in the doctrine of focal infection, not only regarding arthritis, but also regarding many other conditions. The theory has become somewhat unpopular because enthusiasts have pulled out bushels of sound teeth upon false assumptions. That a cure does not always follow the removal of an infected focus is no argument against the theory. It is quite probable that in such cases other foci have been established, and the removal of the original one does not destroy all the sources of infection. In studying a case of arthritis it is absolutely necessary to investigate all possible portals of bacterial entry, particularly the teeth, tonsils and sinuses, but also the prostate gland, the cervical canal of the uterus, the uterine adnexa, the gall-bladder, the appendix, etc.

Focal infection is, however, not the only factor to be considered. There may be predisposing causes in the habits or the occupation of the patient. Endocrine disturbances may also be at work—many cases of arthritis, particularly of the knees, arise at or near the period of the menopause. Our failure to progress in the solution of the riddle of arthritis is in part

due to the fact that we have approached the problem largely by the anatomic route. It is to the credit of Dr. Pemberton and his staff that they have taken the physiologic approach, which when combined with etiologic study promises the best results. I am not sure, however, of the specific importance of their discoveries, I am not certain that the sugar tolerance has etiologic significance, it may be merely an index of something much more fundamental. The same thing applies to the lowered oxygen consumption. But, regardless of their particular significance, the point is that they do throw a certain light on the functional processes in arthritis and will lead without doubt to further research.

To return once more to the question of focal infection: It is evident that besides the bacterial factor there must be another or others. Gonorrhea is common, gonorrheal arthritis uncommon. Not long ago I saw a young man, aged twenty-four years, who had had what appeared to be a mild attack of gonorrhea. In a little while, however, he developed a very severe form of generalized arthritis, which crippled him seriously. Something must have taken place in his system which enabled the gonococci to distribute themselves throughout the body and to settle in the joints. As has been proved in other infectious diseases, besides the seed there is needed the soil. Dr. Pemberton's work concerns itself largely with the soil, with the underlying chemical and physical condition of the patient. It seems to me that in that direction lies promise for light upon one of the darkest fields in medicine.

Dr. Theodore H. Weisenburg: To have a proper perspective of the work of Dr. Pemberton and his associates it is necessary to be familiar with all of their experiments as they have been developed step by step over many years. During the war Dr. Pemberton and a number of physicians had the opportunity of studying 400 cases of arthritis in a hospital in Lakewood designated by the Government for that particular purpose. Among many other interesting findings they found what Dr. Pemberton has been emphasizing this evening, a lowered sugar tolerance. This is found in some neuropsychiatric conditions, but it is noteworthy that as the patient improves the lowered tolerance tends to become normal. Following this work they proved that there was an increased saturation of oxygen in the blood. This, of course, meant that the oxygen did not get to the tissues, and the logical conclusion was that it did not do so because of the lack of circulation, and it was to prove this point that Dr. Pemberton and his associates detailed their experiments of tonight. Conversely, anything which increases the circulation of the tissues, such as massage or electricity, will improve the condition of the part. This has been proved by Dr. Pemberton and his co-workers.

Now my interest in this work lies in the fact that in 60 per cent of the arthritics whom Dr. Pemberton has studied there have been nervous manifestations, such as numbness in the limbs, twitchings, frequently of fibrillary character, headache, migrains and mental symptoms mostly of a depressive character. In the treatment of these patients it has been found that as the arthritic symptoms diminish the nervous symptoms correspondingly

diminish. Now, of course, we all know that there are patients with all these nervous symptoms without arthritis. It is obvious that the same pathology underlies nervous as well as arthritic conditions. It is interesting that in one patient arthritis will develop, in another nervous symptoms, in another skin manifestations, but the broad underlying factor is that the same physiologic disturbance underlies all.

Some metabolic studies have been made in nervous diseases. Two years ago Dr. Schwaat, of St. Louis, reported before the American Neurological Association a lowered sugar tolerance in a great many conditions, particularly in depressed patients. Correspondingly, in the excitable and manic cases the opposite condition was found. While this work is not convincing, it is significant in view of Dr. Pemberton's research.

For many years there has been an effort to explain arthritis by nervous pathology, not unsuccessfully. Years ago I studied the nervous tissues in a case of arthritis, but found no changes. No adequate explanation has ever been offered for the various trophic joint phenomena which are present, for example, in tabes and other spinal cord conditions. We presume there is some disturbance of the sympathetic nervous system, not only in the spinal cases, but also in arthritics, and I think therein lies future investigation. Finally, we ought to be proud of the fact that we have a group of physicians in Philadelphia who are earnestly trying to do good work in what I consider the fundamental basis of medicine.

# THE INTERNAL SECRETION OF THE PARATHYROID GLANDS*

By J. B. COLLIP, M.D.

(Department of Biochemistry, University of Alberta.)

(*Abstract*)

As the work on the parathyroid glands which has been carried out in the writer's laboratory during the past year has been published in detail elsewhere,[1, 5] an abstract only is given herewith.

The status of the parathyroid glands as organs of internal secretion has been amply proven since active extracts of these glands have been prepared, by the use of which complete replacement therapy has been afforded to totally parathyroidectomized dogs.

The active principle elaborated by the glands has been obtained in a stable form and in a degree of purity not hitherto realized.

The manner in which the active principle exerts its effect is not fully understood. The study of the blood chemistry, however, has shown that it exercises a profound influence on calcium metabolism. The injection of the active principle, in adequate dosage, into both normal and parathyroidectomized animals produces a marked rise in the calcium content of the blood. The main action, therefore, of the parathyroid hormone would appear to be related to the regulation of the level of blood calcium.

A method of standardization of the potency of active extracts of the parathyroid glands has been devised. This method is based upon the blood-calcium mobilizing effect of active extracts when injected into normal dogs. A unit of potency has been defined as one one-hundredth of the amount of extract required to produce an average rise of 5 mg. in blood-serum calcium of 20-kilo dogs over a period of fifteen hours. Several animals under dietary control should be used in potency testing.

* Read June 3, 1925.

It has been found that the injection of small amounts of the extract at short intervals (four hours) produces a more profound effect than single injections of equal unitage. Overdosage phenomena, ending fatally, have been produced in dogs by this method of pyramiding.

Overdosage with the active principle in dogs has been attended by a typical train of symptoms, and blood analyses have shown that profound effects are produced in both the chemical and physical properties of the blood.

What the value of the parathyroid hormone will be as a therapeutic agent remains to be determined. A standardized extract is now available, and no doubt clinical studies will shortly determine in what conditions it is of value. It must be emphasized, however, that its use must be attended with great care until more is known about the response of the human subject to injections of the parathyroid active principle.

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## DISCUSSION

Frederick S. Hammett, Ph.D. (by invitation): It is a privilege to be able to discuss this paper and this work of Dr. Collip's. It is particularly a privilege because the work is of fundamental importance. It is of fundamental importance both from the biological and from the clinical or medical point of view. It is obvious that those of us who are working on the biological side are doing work which ultimately, we hope, is going to be of use to the clinicians. The most of our work, however, is not of immediate practical application. The work of Dr. Collip does have an immediate practical application. I will leave the details of that, however, to Dr. Petty to discuss, and will take up a few of the more important biological implications resulting from this work of Dr. Collip.

Before going on, however, I would like to state that while the cat and dog are animals that undoubtedly die if the parathyroids are removed, the rat will not die after complete parathyroidectomy. I will not bother you by going into details of proof of this, but the rat will endure complete parathyroidectomy and continue to live for a long period. Dr. Collip's work is fundamental because he establishes the proof that the parathyroids

are glands of internal secretion and establishes the proof that their function is concerned in mineral metabolism of the body, particularly that of calcium. The work of W. G. McCallum indicated that the parathyroids were concerned with mineral metabolism. It was, however, incomplete proof that these structures were glands of internal secretion. Dr. Collip's work in isolating an active principle from the parathyroids and then injecting this extract into animals deprived of their parathyroids, and getting recovery not only from the obvious symptoms of tetany but also from the disturbance of calcium metabolism, completed the proof that these structures are glands of internal secretion. The importance of this finding of the rôle of the parathyroid function in mineral metabolism is far-reaching. Years ago, from the work of Dr. Lawrence J. Henderson, we believed that the regulation of the mineral composition of the blood was a sort of mechanical affair and dependent upon the regulation of neutrality. Later the work of McCallum, Funk and others introduced the idea that mineral metabolism was related to vitamins. Recently the work of Hess and others has shown conclusively that light, ultraviolet light particularly, is of great importance in the regulation of the mineral metabolism of the body, and of course we all know that the intake of calcium and other mineral salts into the body with the diet is a further important factor. Now Dr. Collip injects another factor into the situation. We have neutrality regulation, we have vitamins, we have light and diet and now parathyroids—all concerned in this phase of metabolism. I believe the importance of the work of Dr. Collip is going to be along the lines of the mineral metabolism of the body. Such being the case, all the individuals working along this line must take into account the significant rôle of the parathyroids. I might state that I have found in my experiments that following parathyroid removal, calcium is lost from the bones. Along with this loss there is an increase in the phosphorus and magnesium percentage of the bones. There is thus evidence of a general disturbance of these three inorganic constituents—calcium, phosphorus and magnesium. Dr. Collip has shown there is a disturbance in calcium and phosphorus of the blood after injection of parathyroid extract. I think this is adequate to show you the fundamental biological importance of this work in connection with what has gone before.

Dr. Orlando H. Petty: It is really a privilege to be permitted to discuss a paper from one so young as Dr. Collip and yet he has been actively associated with two of the epoch-making discoveries within the last three years—the first, insulin, and the second, the parathyroid hormone, the latter wholly the result of his labors.

I am not competent at all to discuss theories or the animal experimentation with Collip's parathyroid hormone. What little discussion I shall give will be of its clinical application, showing especially that it has practically the same effect upon human beings as it has upon dogs. Through Dr. Collip's kindness and the aid of Dr. Walters, of Eli Lilly & Co., who supplied us with the preparation, I and my associates, Drs. Stoner, Schafer and Karr, have been using Dr. Collip's hormone for nearly three months

and we will report a few observations that confirm Dr. Collip's statement that it is the active hormone, showing that it does raise appreciably and measurably the blood calcium in human beings. I think we can best do that by showing a few slides which we have prepared of some of the typical cases. We have encountered a few human beings in whom the doses which we gave did not appreciably raise calcium. The supply was so limited, however, that we were not able to increase the dose in order to decide whether or not they were really refractory to the parathyroid hormone. We used the unit of Dr. Collip and tried to approximate it to the body weight of man compared with dogs. These cases were studied in the Philadelphia General Hospital or in the Memorial Hospital and the blood calcium work was done in the associated laboratories of the two hospitals. The time being limited for the discussion, I think we can best show our results with slides prepared from typical cases.

This slide shows the highest elevation of blood calcium which we observed. You see the blood calcium was 11.7 before administration of the hormone. A total of 270 units was administered in six days and the blood calcium rose to 16.8 mg. per 100 cc. of serum. This patient had no symptoms of hypercalcemia, although some of our patients showed definite toxic symptoms when the blood calcium was raised 3 or 4 mg. per 100 cc.

Slide No. 2 shows an elevation of calcium from 9.7 to 13, 80 units being administered.

Slide No. 3 is the record of a cretin, aged twelve years. Her blood calcium before administration of the hormone was 9.4. After hormone administration it went as high as 13.6.

Slide No. 4 shows an elevation from 9.6 to 13.9. This was a severe advanced case of arthritis deformans. The calcium administration was continued for several weeks. No good effects were observed.

Slide No. 5, a diabetic, shows an elevation from 9.6 to 12.6.

Slide No. 6, pernicious vomiting of pregnancy, shows an elevation from 9.6 to 13.1.

The slides just shown are typical of the majority of cases upon which we have used the hormone and we are glad to confirm Dr. Collip's statements of his experiment upon dogs. We have used this preparation upon cases of chronic ulcer which had failed to respond to the usual treatment, also upon ununited fractures of several months' duration, chorea and hypertension. We do not feel justified in making any statements as yet concerning the clinical usefulness of Dr. Collip's parathyroid hormone except to endorse the statement made by Dr. Collip that its use is probably indicated in every case of deficiency of secretion of the parathyroid hormone.

# THE FUNCTION OF A MEDICAL DISPENSARY*

By TRUMAN G. SCHNABEL, M.D.

The medical dispensary or outpatient medical department of a hospital is now an institution of long standing and by reason of its valuable service to the community needs no defence for its existence. Instituted as a means of caring for the indigent ambulatory sick, such departments for a long time occupied a very insignificant place in the physical side of our hospitals, and those who carried on the work often did so with the expenditure of a minimum amount of time and effort. As time has passed the dispensary has broadened its field of activity and has assumed a more and more important rôle in hospital endeavor. Commodious and well-equipped quarters are now set aside for outpatient department activity and physicians are devoting an increasing amount of time and attention to this work. Instead of a few hours, half a day or even a whole day is given to the dispensary. This development has happened with the course of events in medicine at large and has been the resultant of numerous influences: Not the least of these has been exerted by hospital managements, physicians and others as they have recognized that the great opportunity in medicine lies in the guidance of those suffering from no illness whatever, in the early detection of disease and in the care of those suffering with difficulties of comparatively recent origin. The dispensary, occupying as it does the outpost position in this crusade for health and against disease, has quite naturally been the part of the hospital that has received much stress in recent years. In view of the fact that the new attitude toward dispensary usefulness is not widely appreciated, it would seem timely to state what the scope of the outpatient department work has come to include, how and by what means it achieves its purposes, and then to touch upon some special phases of dispensary conduct.

* Read June 3, 1925.

Primarily the work of this hospital department, in common with the entire hospital, is concerned with the care of the sick. This necessitates the diagnosis and treatment of disease. The former of these procedures is brought about by careful history-taking and physical examination. This work can only be done by a doctor or perhaps, under direction, by student clerks. Certain data, chiefly related to the social and financial status of a patient, can be ascertained by nonmedical assistants; often the social-service worker helps in this matter. The diagnosis is further achieved by consultation with other outpatient departments and the utilization of certain clinical aids either of the laboratory or of instrumental precision.

The treatment of patients is carried on by the prescription of various drugs and by hygienic, dietetic and other advice of the attending physician; quite often social-service agencies may be called upon for help and suggestions. Besides these means there are hydro-, mechano-, electrotherapeutic methods available for treatment, and the facilities of surgery can after proper study be called upon for its beneficent aid. If a diagnosis is not reached by daily observation or satisfactory therapeutic results are not accomplished, then hospitalization or other disposition is made of the patient.

Dispensary efficiency has been considerably increased by classification of cases in special groups. For example, a subdivision of the medical dispensary is made into that part which deals with gastrointestinal cases, heart cases, lung cases, metabolic cases and in some instances a subdivision is made into the so-called health clinic. Those who have charge of these special groups become increasingly efficient in the care of the disease included under their special heads and opportunity is afforded for specialistic investigation and more intensive treatment.

Obviously, all of this differs in no respect from the generally accepted procedure of diagnosis and treatment in private practice or in ward service. The hospital dispensary, however, offers a peculiarly happy opportunity of arriving at the desired end in cases unable to economically meet the cost of such service when practised by a private physician. The hospital dispensary gives to the poor the sort of study and care which all of our patients should receive.

To accomplish all of these aims there must be close coöperation

between all concerned. The patient is the focus of attack carried on by nurses, social-service agencies, members of the house staff, both visiting and resident, dispensary physicians, convalescent homes and family doctors. The interrelationship between these workers is maintained by personal interview and consultation, written communications and well-executed reports and records. All of this means that, in addition to the usual professional personnel attached to a dispensary, there must also be those who direct patients in their journey about the hospital, those who catalogue and care for histories and those who do secretarial and stenographic work.

The conduct of a dispensary must, of course, in its details be adapted to local conditions, depending upon whether or not the clinical material is utilized in teaching, upon the physical equipment of the dispensary and upon local custom and usage.

Not less important than the care of patients is the educational function of the dispensary. Naturally the attending physician reaps a valuable experience in his daily work. His education is effected by the study of his patients, by the teaching of nurses, medical students and visiting doctors, and by the great opportunity for research. Each day finds an ever-increasing utilization of outpatient material for this very important work. In teaching hospitals, of course, the medical student finds a great opportunity for practical experience. He serves as a clinical clerk, examines patients, executes certain laboratory tests, carries out certain clinical methods of investigation and, of course, in this matter as in all others, tentatively prescribes and advises patients. Besides all of this, he observes how medicine should be practised and what progress patients make from time to time. He is observing the sort of material with which he will be required to deal when he assumes the practice of medicine for himself. Nurses and social-service workers can be well trained and educated here either by way of personal experience or by didactic instruction. Here, too, the family doctor, the doctor of the community, may send patients for consultation and in turn receive reports, diagnoses and suggestions for treatment. He can further enhance his knowledge by personal work in outpatient departments and by observation and attendance upon didactic talks. Patients themselves can share in the educational advantages offered by dispensary services. Their mode of life may be properly directed, either individually or in class groups.

Class instruction is now conducted for such diseases as diabetes, tuberculosis, heart disease, etc. Through these patients, in turn, their families are educated and thereby the entire community is touched by the medical dispensary.

With any discussion concerning dispensaries there always arises the question of dispensary abuse. This is an event which should not occur in a well-conducted modern dispensary where conscientious people carry on and where careful economic investigation is conducted before the patient is admitted. Such an investigation should ascertain whether or not the patient has received treatment at other dispensaries or by other physicians and, if he has, should be returned with or without a consultation opinion. In most instances he should not be admitted without the consent of his physician or the dispensary where he last received treatment. The same ethical relationship must hold between dispensaries that holds between physicians. Naturally, mistakes will occur in dispensary work just as they do in the relationship of physician to physician.

The question of the propriety of pay clinics is one which is much discussed today. Time will probably solve this matter and individual communities will probably solve the question for themselves. Undoubtedly there are many people who can pay a moderate sum for medical services which could not be procured for the same amount under other circumstances. In paying a moderate fee they maintain their self-respect. It does seem that every sick individual should be given an opportunity to receive the best that modern medicine can offer.

Who should work in this important part of the hospital is another question which suggests itself. The best results seem to be obtained when the same staff serves both in the hospital ward and outpatient department. Those dispensaries are the most efficient when the hospital chief keeps in touch with his dispensary, best of all by visitation and consultation. A service which operates both the in- and outpatient department makes for the best and most easily maintained relationship between these parts of the hospital. A dispensary can also be a medium for the trial, so to speak, of medical candidates for staff positions. A system of promotion helps materially to maintain a healthy interest.

The question of remuneration for services in the dispensary is another important one. If the physician takes full advantage of his work in a good outpatient department he receives much in

return for his efforts which is not measured in dollars and cents. On the other hand, the economic stress of our present-day life and the financial inducement coming from industrial medicine and other sources make the appeal of volunteer dispensary work to the young doctor rather unattractive. This is unfortunate and is not true of all communities. In some instances all hospital physicians are on some sort of a pay basis. Pay clinics are, of course, in a position to offer some remuneration to their workers. It would seem that sooner or later some pay scheme must be instituted in all dispensaries both for the patient as well as for the doctor.

It was earlier suggested that one of the most recent functions of the medical dispensary is that of caring for those who have no disease. In this capacity it can best serve the individual and the community by affording an opportunity for periodical health examination. In this matter the poor should be more thoroughly educated. The farreaching benefits to be realized by such a practice needs no emphasis in this paper. This single function of the medical dispensary it would seem alone justifies the increased physical equipment devoted to this present-day department and the increased amount of time expended by physicians. As I have tried to point out, however, beside this single educational phase of dispensary practice there are numerous other educational possibilities, to say nothing of the time-honored function of the care of the indigent or comparatively poor sick of the community.

The modern medical dispensary, then, differs from its former self in the increased amount of time being devoted to the study and care of patients, in the increased utilization of clinical aids in diagnosis, in having the coöperation of social service with all its possibility and in offering an opportunity for clinical research. It also offers increased amount of educational possibilities for all those who come in contact with its influence either directly or indirectly. These possibilities are farreaching and increasing in scope. It offers today an enlarged measure of opportunity for the maintenance of health in the community, the early detection of disease and its prevention.

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## DISCUSSION

Dr. O. H. Perry Pepper: It is very desirable to fix our thoughts on the dispensary occasionally. It is often neglected, left alone, and attention is too much focused on the other half of the institution. Dr. Schnabel

has mentioned a few of the many points that could be mentioned in favor of dispensary work over a period. There are several I want to add:

One of these concerns the relative economic, the relative cost in the treatment of a patient in dispensary and the treatment of that same patient in a hospital on a free basis. The cost of treatment in a hospital is enormous today, enormous to the patient if he tries to pay the ward-rate, enormous to the institution if it tries to take in the patient. Much can be saved by treatment in dispensary.

Second, I wish to raise the question as to whether the modern dispensary should be the place for teaching of the third- or of the fourth-year students. In several medical schools of which I know the third-year students get their work—I am speaking now of medicine—in the medical dispensary. The fourth-year men get their work in the wards, just the opposite to custom in other places.

The third point, as to economy, is dependent upon what constitutes a dispensary. I certainly disapprove of the modern tendency of making of the dispensary a small hospital within the main hospital. I know some dispensaries that have wards attached to them with two or three beds, and their own laboratory and *x*-ray departments. At the same time that the expense is increased you are losing the desirable similarity of the dispensary to private office practice. Under such conditions it does not make very much difference whether the third- or fourth-year students receive their teaching in the dispensary. Personally, I think the third-year students should go to the dispensary and the fourth-year to the wards, the third-year men should also visit the wards and the fourth-year man should renew touch with the dispensary, and, just so, the dispensary staff should keep in touch with the ward work and the ward staff should renew theirs with dispensary work.

Dr. Schnabel spoke of the plan of promotion which might be put into effect from the dispensary to the ward staff. I would wish to disagree with him on that. The ward staff and the dispensary staff should form a whole, they should be the staff of the hospital as a whole, and promotion should be upward in the staff irrespective of where the individual's duties might be.

Dr. Robert G. Torrey: I believe that Dr. Schnabel's paper is timely. The work of the medical dispensary differs from that of the ward, not being less important, but being different: The medical dispensary treats chronic disease where the ward treats acute disease. The work of the medical dispensary is probably not for months or weeks, but years. A long period of years. If the medical dispensary is to be successful it must have the right type of social worker and the right type of physician. The physicians cannot be secured by the payment of small fees, entirely inadequate for that type of men. They can be secured by coöperation of the hospital. The hospital must furnish adequate laboratory service to take care of these patients. The laboratory and real social service must be taken care of by an adequately salaried service. If that is done I do not think there will be any difficulty in getting men with proper qualifications to take care

of the medical dispensary. You cannot get a man year after year to give three or four days a week to dispensary work, but it is possible to get good men who are willing to give the time necessary to conduct the dispensary one day a week if the laboratory and social service departments are well taken care of.

Dr. Stanley P. Reiman: My remarks will be confined to that phase of the question interesting to the laboratory. The laboratory can be useful to the dispensary and the dispensary can be useful to the laboratory. We need but mention, to pick up threads from Dr. Schnabel's discourse, the aid in detecting early manifestations of disease in patients who report because they feel sick or because they feel that a health examination is a wise procedure. I need not call to the attention of this body that the urine can be examined for albumen, sugar, pus, casts, etc., that suspicious sores can be investigated for spirochetæ, that cultures can be made of wounds or of skin diseases, that vaccines can be made and so on. The laboratory can learn and better establish the earlier signs of disease through efficient continuous observation of patients. Diagnosis of lesions can be made on biopsy specimens, although we must emphasize that this procedure is not to be recommended routinely in neoplasms or even in neoplasm-like conditions. We feel, furthermore, that, especially in such conditions but very often also in other diseases, the pathologist can be asked in consultation with profit not only to the patient but to the attending physicians and the pathologist himself.

In our hospital there is established a well-organized follow-up department in which we are happy to say that fully 85 per cent of our house patients have reported at least once and in many cases many times. The pathologist is interested in this department from all angles, because there are the questions of neoplasms, the return or absence of symptoms following such conditions as gall-bladder disease, gastric ulcer, heart and kidney decompensations, and so on, in which broad pathological problems are involved. It is brought home very strikingly in a follow-up department that a very large percentage of follow-up treatment, perhaps even 50 per cent or more, is social and not medical. In our particular case we have made every effort to send our patients back to the physicians who have referred them to us, but there are a number who either have no family physicians or for one reason or another do not wish to return. In deserving cases the dispensary is the place for them to go. Thus the dispensary has been a great aid in starting these patients upon the right track, and has naturally thereby assisted us in our efforts to study the patients and thus make them derive the greatest benefit possible from our studies.

Finally, the concrete method by which the laboratory can be of assistance will differ according to the size of the clinic and the general way in which the laboratory work of the hospital is carried out. In many institutions, as in ours, all of the laboratory work is done in a central place. We have thought that the best way to assure speedy coöperation is to assign one of the workers, a technician, to do the laboratory work needed by the dispensary on the particular days and hours at which the clinic is held. An

experienced worker can thus examine specimens of urine, blood, gastric contents and so on immediately, so that the physicians can have the results reported usually on the same day. A diabetic, for instance, can thus obtain the proper advice as to diet and so on with a minimum of effort. This scheme makes for accuracy, completeness, maintained interest and, what is very important many times, it saves extra and unnecessary visits to the dispensary, which in many cases involve loss of time from work or loss of time from home and children in the case of mothers.

WILLIAM W. KEEN, M.D.

# ADDRESS ON PRESENTING A PORTRAIT OF WILLIAM W. KEEN, M.D.*

By WILLIAM J. TAYLOR, M.D.

I ESTEEM it a very great honor to be asked to present this portrait of our former president, Dr. W. W. Keen, as a gift from his daughters. He is shown in the red robe of St. Andrew's University, where he was given a degree at its five-hundredth anniversary in 1911; over this is worn the three bands of white fur, the "epitoga" of the *doctor honoris causa* of the University of Paris. He is the sixth American to be given this degree.

It is very difficult for me to find words adequately to describe the honors which have been heaped upon him by educational and scientific bodies throughout the world. Elected a Fellow of this College in 1867, he was made president in 1900 and, since serving his term of office, has been a censor. He has been president of the American Surgical Association, president of the Philadelphia Academy of Surgery, president of the American Medical Association and president of the American Philosophical Society. For many years he was professor of the principles of surgery and clinical surgery in the Jefferson Medical College, his alma mater. He is an associate member of the Academy of Medicine of Paris, honorary member of the Society of Surgery of Belgium, honorary fellow of the Royal Society of Medicine of London and was president of the International Society of Surgery in 1923. He has been given honorary degrees without number: Doctors of Law; Doctor of Science; Honorary Fellow, Royal College of Surgeons of England, Edinburgh and Ireland, and of the American College of Surgeons. He has been decorated by the king of Belgium, with the order of Leopold; by the president of the French Republic, as an officer of the Legion of Honor, and, what he prizes very highly, are medals

* Read June 3, 1925.

definite significance that they all followed abdominal operations. Since this report 48 cases have been reported in literature. In January 1925, Scott[53] had collected 64 cases.

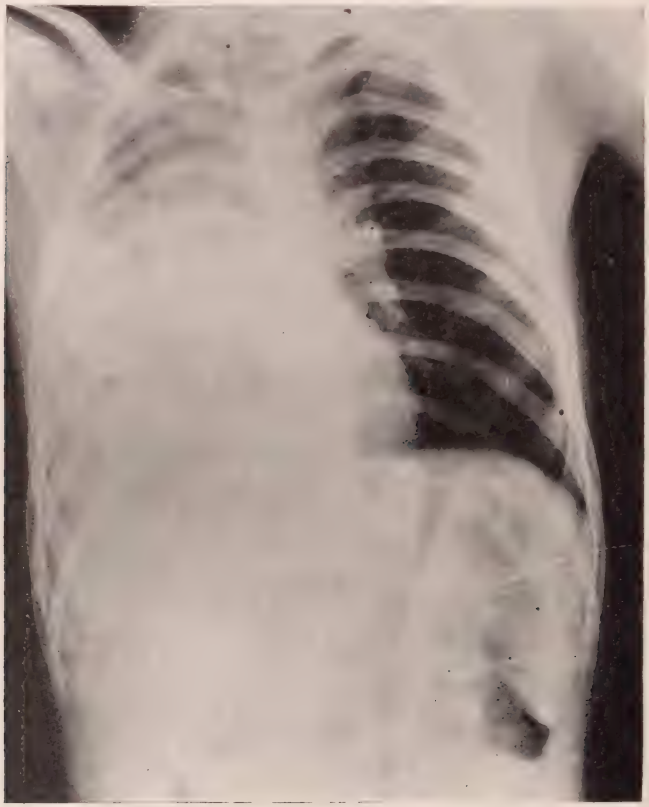

FIG. 1.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken three days after the drainage of an appendiceal abscess by Dr. Davis and ten hours after the onset of the clinical symptoms of acute massive pulmonary collapse. Massive collapse of the middle and lower lobes of the right lung. Partial displacement of the heart to the right. Displacement of the trachea to the right. Radiograph by Dr. Henry T. Thissell.

Pasteur would have us confine this term to a condition of massive collapse in which the alveolar portion of the lung is completely deprived of its air. When incompletely airless he suggests the term "partial deflation." This seems to us to be unnecessarily confusing. Undoubtedly varying degrees of pulmonary collapse

occur, and Briscoe states it is his belief that a large majority of postoperative pulmonary symptoms are entirely due to varying degrees of pulmonary collapse. To us its clinical importance as a postoperative complication lies not in the occasional massive collapse that is encountered, but in the frequent partial collapse of

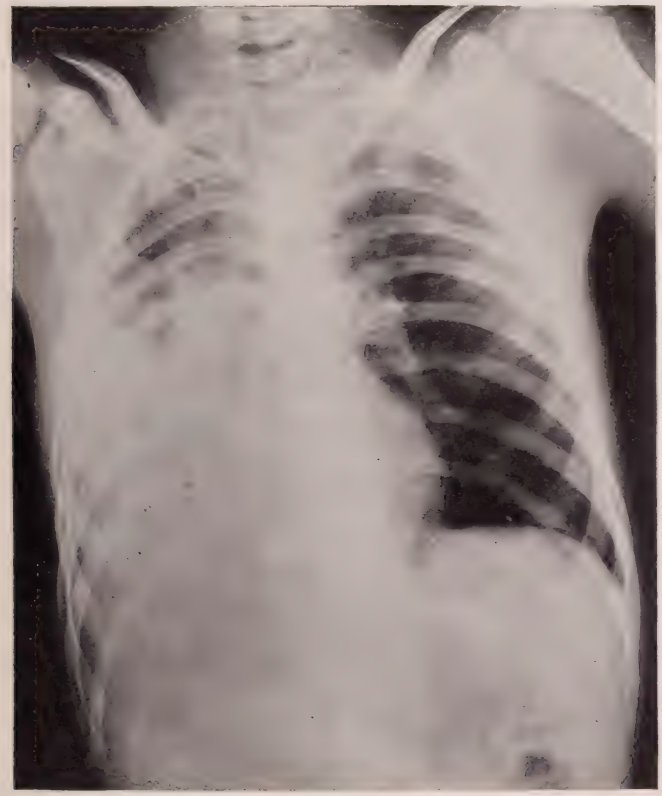

FIG. 2.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken twenty-four hours after the onset of the clinical symptoms of acute massive pulmonary collapse. A slight increase in the amount of air in the right upper lobe since the taking of the last picture, but the heart has moved further to the right. Radiograph by Dr. Henry T. Thissell.

varying degrees after certain types of operative procedures, trauma and other conditions of which we will speak later. However, up to the present time only massive collapse has been demonstrated, but we hope to be able to confirm our inference concerning partial collapse.

The occurrence of this phenomenon has been described (since Pasteur's original report) associated with or following many conditions. Thus Norris and Landis speak of massive collapse of the lung as a complication of pneumonia. Rose-Bradford[19] report

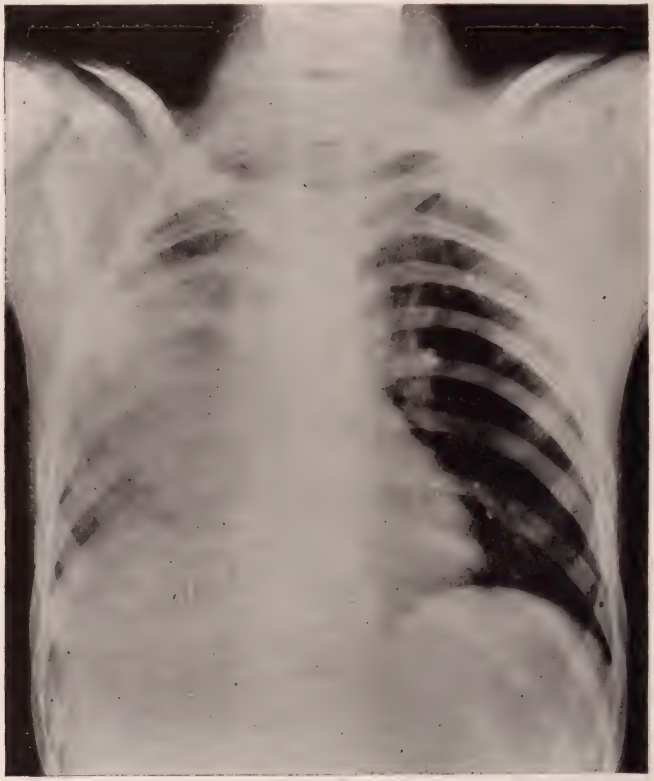

FIG. 3.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken two days after the onset of the massive pulmonary collapse of the middle and lower lobes of the right lung and on the fifth postoperative day. This picture was taken immediately after bronchoscopic drainage of the obstructing mucus from the bronchi of the right, middle and lower lobes. The middle lobe contains less air than the upper and lower lobes, both of which contain a larger amount than before the bronchoscopic drainage. The heart has also moved to the left and the level of the right diaphragm is almost normal. The trachea is in the midline. Radiograph by Dr. Henry T. Thissell.

the autopsy of such a case. Tidy[21] reports an undoubted case of massive collapse of the entire right lung in a case of diaphragmatic pleurisy. Jorg,[49] in 1832, Legendre and Boilly, in 1844,[49] and Reynolds, in 1871, described the airlessness of the lungs of newborn

children. Reynolds[22] called the condition apneumotosis, or, as we now speak of it, atelectasis. He was convinced at this early date that the distribution of the affected lobules had a direct relation to the bronchial tubes, lobules supplied by one particular bronchial tube often presenting characteristic lesions, while lobules supplied

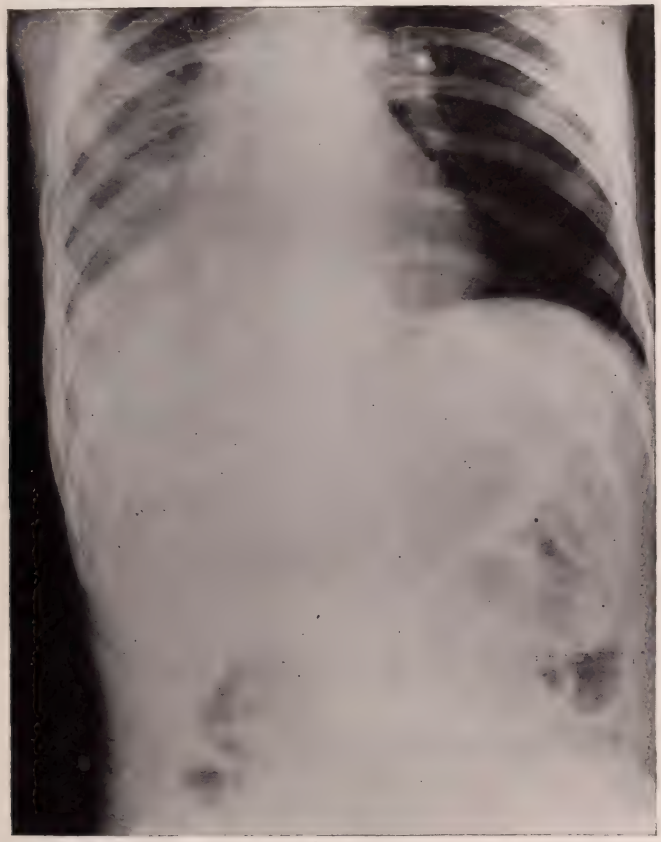

FIG. 4.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken fifteen minutes after the taking of Fig. 2. Radiograph by Dr. Henry T. Thissell.

by closely adjacent tubes may be perfectly healthy. In his mind this precluded the possibility of an infection spreading by simple continuity. The literature contains the largest number of references to this phenomenon occurring after diphtheria, as originally described by Pasteur. The military surgeons supply the next

largest group in those following trauma, especially following unilateral wounds of the thoracic wall and occasionally wounds of the buttocks, pelvis and thigh. Finally there is an increasing incidence in the surgical literature as its relation to operative procedures, especially upon the abdomen, is becoming appreciated.

FIG. 5.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken twenty-four hours after the bronchoscopic drainage of the obstructing mucus in the bronchi of the right, middle and lower lobes and three days after the onset of the massive pulmonary collapse of these lobes. The reaccumulation of mucus again obstructs the bronchi and the collapse of these two lobes is almost as great as Fig. 1. Radiograph by Dr. Henry T. Thissell.

1. Thus this condition may develop as a: (1) Congenital deformity (as in apneumatosis in the newborn); (2) it may develop spontaneously (as in diaphragmatic pleurisy); (3) it may follow infection in the lung or the bronchi (as in pneumonia and purulent bronchitis); (4) it may follow nonpenetrating traumatisms of the chest and of the adjacent abdominal wall, buttocks and pelvis; Chevalier Jackson[50, 51] has demonstrated its occurrence in cases of foreign bodies in the bronchi and it has an approximate incidence of at least 8 per cent after abdominal operations. For such varied con-

ditions it would seem difficult to find a common etiological factor. This is apparently true, judging from the discussion of its etiology that appears in recent literature.

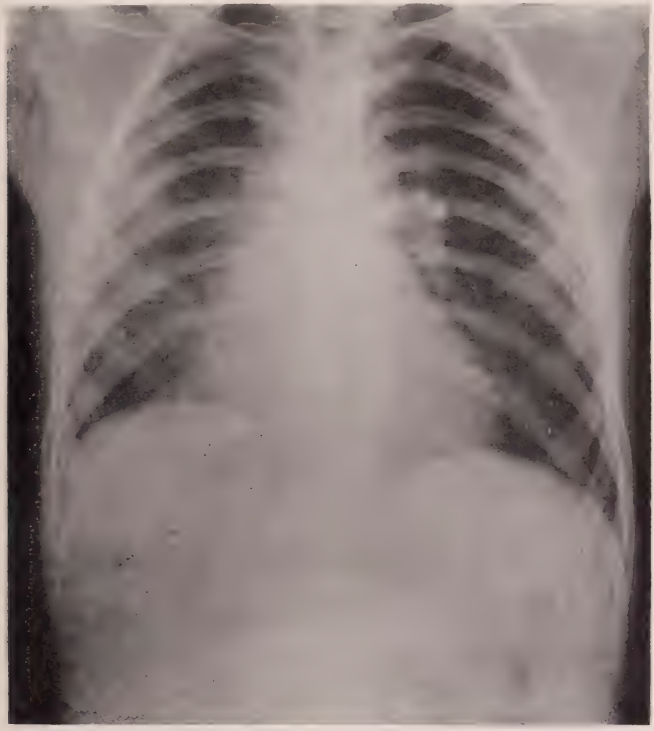

FIG. 6.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken two days after the first bronchoscopic drainage of the obstructing mucus and just before the second bronchoscopic drainage. This was three days after the onset of the symptoms of massive pulmonary collapse. In the preceding twenty-four hours there had been a copious expectoration of thick tenacious mucus similar to that removed through the bronchoscope. The air capacity of the lungs is now almost normal. The heart has returned to its normal position and the trachea is in the midline. Radiograph by Dr. Henry T. Thissell.

A careful analysis of these apparently diverse conditions with which massive pulmonary collapse is frequently associated shows two factors to be practically constant.

2. Obstruction of the bronchial tree, which is followed by the absorption by the pulmonary circulation of the imprisoned air in the alveolar tissue distal to the obstruction.

3. Some interference with respiratory movements. This interference may be partial or complete but always results in decreased aëration of the pulmonary tissue on the involved side.

Fig. 7.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken four days after the first bronchoscopic drainage of the obstructing mucus, and it shows almost complete restoration to the normal. This examination was made immediately before the second bronchoscopic examination by Dr. Tucker. Radiograph by Dr. Henry T. Thissell.

Obstruction in the Bronchial Tree. The effect of such an obstruction was first demonstrated experimentally by Mendelsohn[49] in 1845, and later by Lictheim[26] in 1878, but the clinical work of Chevalier Jackson and his assistants in the removal of foreign bodies

impacted in the bronchi has established this phenomenon beyond the possibility of controversy. Jackson states that this obstructive atelectasis has been shown by Manges[54] at the Bronchoscopic Clinic to be a most valuable means of diagnosis of nonopaque bodies in the bronchi. The similarity of the clinical symptoms and the roentgen-ray pictures before and after the removal of foreign bodies through

FIG. 8.—C. L., patient of Drs. Walter Estell Lee, Gabriel Tucker, Harry Wilmer and Howard Geissler, Germantown Hospital. Picture taken one hour after Fig. 7 and immediately after second bronchoscopic examination by Dr. Tucker. There is a complete retoration to the normal of the pulmonary tissues and the position of the heart. This is four days after the bronchoscopic drainage of right lung. Radiograph by Dr. Henry T. Thissell.

the bronchoscope with the findings in the massive collapse encountered in postoperative pulmonary complications has impressed us for some time. Jackson was the first to call attention to this, and Leopold[44] in his report speaks of Jackson's suggestion that possibly a bronchoscopic examination might not only determine its etiology but also serve as a therapeutic procedure. We have previously reported a case,[43] our first one, where at autopsy by Belk a definite

postoperative collapse was found of the lower right lobe of the lung with a purulent pneumonia of the upper two lobes. In tracing the bronchus of the lower lobe a definite plug of organized or agglutinated purulent mucus was found which completely blocked the pulmonary tissues served by it. Though in our first report we recorded this finding, we reproduce here the photograph of the

FIG. 9.—A roentgenogram showing massive collapse of the lung from bronchial obstruction, Type III; stop-valve obstruction. Air can get neither in nor out because of the presence of a nonopaque plug (a bean) in the right lung. Absorption of the trapped air has resulted in acute massive collapse of the right lung. This condition which we call "obstructive atelectasis" is of almost daily diagnostic usefulness at the Bronchoscopic Clinic. Often the patients come in with an erroneous diagnosis of "pneumonia;" which is parallel to the similar error in postoperative collapse.

specimen and the pathological report because, in a recent bronchoscopic examination by Tucker (to be later reported in detail), similar plugs of mucus have been found in the bronchi of an acute massive postoperative collapse of the lung. The removal of these plugs through the bronchoscope allowed the distal pulmonary tissue to reëxpand with air, as was proven by the roentgen-ray taken by

Thissell and the clinical examinations of Geissler and Wilmer. When the clinical and Roentgen-ray examinations demonstrated a return to normal of the previously collapsed lung, a bronchoscopic examination demonstrated the disappearance of the mucus plugs that had been previously found. To us this would seem conclusive evidence that obstruction of the bronchi by foreign bodies or by mucus plugs may produce varying degrees of pulmonary collapse

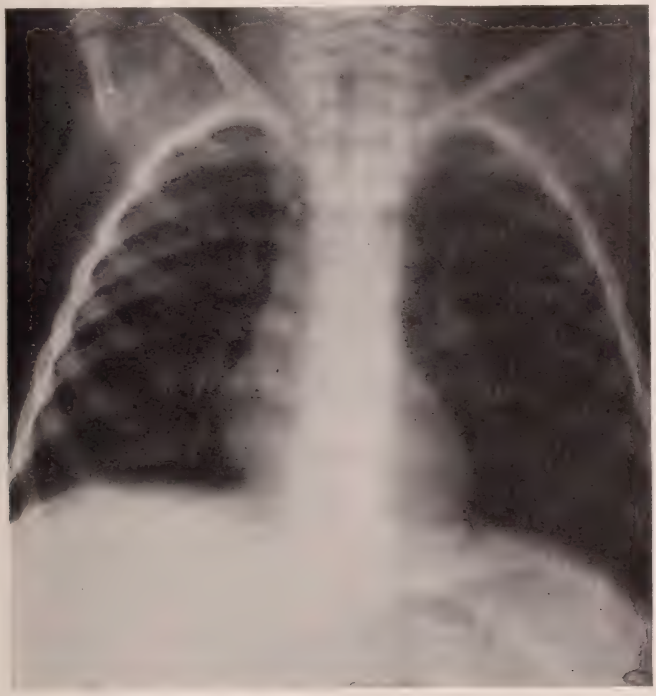

FIG. 10.—Roentgenogram of the same patient three days after Dr. Gabriel Tucker removed the obstructive bean. The collapsed lung is expanded and is functioning normally.

according to the character of the foreign body and to the completeness of the obstruction of the bronchi by the mucus plugs. Manges, from his experience with foreign bodies, states that atelectasis or collapse does not occur until such a time as the obstruction is complete to inspiration. If the obstruction is incomplete, then, instead of atelectasis, we will have the tissues beyond the obstruction overdistended with air. This may be the explanation of the two

distinct clinical groups into which postoperative massive collapse may be divided.

1. In one, over the area occupied by the collapsed lung, there is hyperresonance and even tympany, the vocal fremitus is increased and the breath sounds are loudly tubular or amphoric, while bronchophony and pectoriloquy are well marked. Here we may have incomplete obstruction to inspiration.

2. The clinical symptoms in the second group are exactly the opposite: Vocal fremitus is diminished and the breath sounds are absent over this area and the atelectasis is complete, as we would expect in a sudden and complete obstruction of the bronchi.

The other factor common to conditions in which acute massive collapse of the lungs is associated is partial or complete arrest of the respiratory movements. Thus in pleurisy, pneumonia, diphtheritic paralysis of the diaphragm, reflex inhibition or voluntary fixation of the diaphragm and abdominal muscles in upper abdominal operations, this mechanism is obvious. Just as important and more constant is the embarrassment of respiratory movements resulting from unnatural and prolonged rest after abdominal operations and other operative procedures and accidental injuries. The contralateral collapse associated with nonpenetrating wounds of the opposite chest wall, which was found so frequently during the World War, Tidy explains by the patient's lying upon the well side and thus immobilizing its respiratory movements.

Decreased aëration probably results in an increase in the bulk of the bronchial secretions because of decreased evaporation. These secretions gradually increase and accumulate in the larger bronchi and when a point is reached where the tidal air is insufficient to maintain an airway and the cough reflex fails to expel the mucus the lumen will become completely obstructed. When this does result we have the mucus plugs acting exactly as a foreign body. Jackson, in several recent contributions, has called attention to the normal function of the cough reflex. As he expresses it: "The cough reflex is the watchdog of the lungs." In view of this function we ask you to consider the effect of posture, severe postoperative abdominal pain and the generous pre- and postoperative use of morphia upon the expulsive cough necessary to clear the bronchial tree of secretions.

All this was clearly suggested by Elliott and Dingley in 1914.[27] As our present contribution to the subject we state: (1) That

we have been able to find such obstructing plugs postmortem; that we have seen such plugs *in vivo*, and that one of us (Tucker) removed them through a bronchoscope and proved that after its removal the lung returned to its normal condition; (2) the suggestion of Briscoe,[18] Elliott[27] and Dingley and Elwyn,[40, 41, 42] that embarrassment of respiratory movements of the chest-wall or the diaphragm is a predisposing factor not only in the formation of the mucus plugs in the bronchi but in the inability to expel them, has been entirely confirmed by our clinical experience. (3) That this phenomenon has definite surgical significance. To us its importance as a postoperative complication lies not in the occasional massive collapse that is to be encountered, but in the probable frequent collapse of varying degrees occurring after operative procedures, particular abdominal, and traumatism of the trunk. (4) That the arrest in these collapsed areas of the small emboli which are usually scattered through the circulation after all operative procedures, as proven by Cutler[1, 2, 57] is an explanation of the mechanism of postoperative bronchopneumonia. The clinical picture of the so-called cases of postoperative or postanesthetic pneumonia is so unlike the true lobar and lobular pneumonias which are seen by the internist and physician that it is strange we have so complacently accepted this diagnosis up to the present time.

Conclusions. 1. Acute massive collapse or massive atelectasis is a phenomenon which has been recognized associated with many conditions. Although diverse, they have two factors in common which we believe have some bearing upon the etiology of pulmonary collapse, namely: (*a*) Embarrassment or paralysis of the respiratory movements and (*b*) obstruction of the bronchial tubes. The interference with the respiratory movements may be as slight as that resulting from posture and increase to that of the voluntary or reflex inhibition from the postoperative pain of abdominal operations or reach the complete paralysis occurring in diphtheria. Obstruction has been found to be caused by foreign bodies, bronchial secretions or extrabronchial pressure, such as is produced by tumors.

2. Massive collapse of the lungs is a comparatively rare condition and its incidence postoperatively is approximately 8 per cent. However, it has a definite surgical significance and should not be overlooked. The most characteristic sign is the displacement of the heart toward the collapsed lung.

3. Partial collapse of the lungs is probably a very frequent

complication following abdominal, and particularly upper abdominal operative procedures. The arrest in the areas of partial collapse of multiple emboli coming from the operative field is probably the mechanism and the lesion which so frequently occurs after operative procedures and which is commonly called postoperative or post-anesthetic pneumonia.*

4. When infection is added to the minute multiple infarctions in the collapsed area a true bronchial pneumonia is established. This, we believe, is rare compared to the frequency of partial collapse combined with minute pulmonary emboli and infarction.

5. If two of the factors underlying pulmonary collapse, either massive or partial, are inhibition or arrest of respiratory movements and subsequent obstruction of the bronchi with accumulated bronchial secretions, there are definite indications for prophylaxis and treatment. The minimizing of the trauma of all operative procedures; the conservative use of morphia and other inhibitors of the normal cough reflex; and the avoidance of fixed or unnatural positions postoperatively would seem rational procedures. The choice of such anesthetic agents as have the least irrigating effects upon the bronchi and result in the minimum of bronchial secretion, as local anesthesia and gas-oxygen anesthesia, are mandatory. All these measures are prophylactic. After the condition of massive collapse is established the dangers are not in the lesions itself, unless it be bilateral, but in the complications which are apt to ensue, as pneumonia in one of our cases, empyema and lung abscess. The fact that of the recorded cases that have recovered spontaneously the average duration of the recovery has been about twenty-one days and that in the case here reported seventy-two hours after the removal of the obstructing bronchial secretion the lung had been restored to its normal condition is at least suggestive.

* This explanation of the etiology and pathology was suggested by us in a discussion of postoperative pulmonary complication before the Philadelphia Academy of Surgery, November, 1923.[43] Scott[53] has since reported that Finney found post-mortem emboli and infarctions in atelectatic areas of a patient dying of postoperative pulmonary complications.

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## DISCUSSION

Dr. Thomas McCrae: This is an important communication because it explains the mystery in the etiology of certain cases of massive collapse of the lung. There is one point in the paper which might be mentioned.

Dr. Lee emphasized the occurrence of collapse of lung in nonpenetrating wounds of the thorax. It is important to remember that in penetrating wounds of the thorax there may be collapse of the lung on the other side. This study explains the occurrence of collapse in certain cases, namely, with bronchial obstruction, but these are probably only a part of the group. The clinical picture of collapse of the lung due to complete bronchial obstruction is very definite, and in certain cases of collapse of the lung the signs do not in any way suggest complete plugging of the bronchus. In certain cases of collapse of the lung the vocal fremitus is increased and the breath sounds are loud and perhaps almost amphoric. How many cases of collapse are due to plugging of a bronchus will have to be determined by bronchoscopy. We have been slow in waking up to the fact that many of the postoperative pulmonary complications are due to lung collapse. I do not think there is any doubt that pneumonia does follow anesthesia or operation, but undoubtedly we have diagnosed collapse as pneumonia. This study explains certain of the cases, but how many shall we have to decide by careful teamwork between the surgeon, the internist, the radiologist and the bronchoscopist?

Dr. David R. Bowen: I think that we are much indebted to Dr. Lee and Dr. Tucker for this contribution to a subject which has only recently become of importance, from an *x*-ray standpoint at least. There is no mention of massive collapse of the lung in the *x*-ray literature previous to about one year ago. The pointing out of this factor of bronchial plugging is wholly new to me and is apparently of extreme importance.

There has been much confusion among good men in *x*-ray circles as to just what this condition is. It seems so illogical to speak of collapsed lung when no air has entered the pleural cavity. Ordinarily in collapsed lung we find the pleural cavity on the affected side filled with air. In this condition the space in the affected side normally occupied by the now collapsed lung is occupied by the encroachment of the emphysematous lung from the opposite side. That accounts for the unusual position and motions of the heart.

It seems that the paucity of *x*-ray literature on this subject is largely or entirely due to the fact that *x*-ray men have not seen these patients. Surgeons do not willingly send recently operated patients to the *x*-ray room under ordinary conditions and until practically the close of the war there were no really efficient bedside units. For these reasons *x*-ray examinations of these patients were not made. It seems that much is to be expected now that, with modern bedside apparatus, we will doubtless have greater opportunity to study recently operated patients, in many of whom this condition may be expected.

That will undoubtedly, as Dr. Lee has pointed out, reveal many cases of partial collapse. I see no reason why we should not use the term collapse, because it is collapse just as truly as the classical cases with pneumothorax, the actual condition of the lung being practically the same whether the extrapulmonary air is within the pleura or in the emphysematous opposite lung.

In the hospital where my work is done we are handicapped by an inefficient current for our bedside apparatus and our exposures are too slow for good lung-studies. But we have a rather superior way of handling very ill patients when we do take them to the *x*-ray room. We use a wood-frame, canvas-top stretcher quite loose from its carriage, so that it can be lifted off and placed beside the patient on his bed. Once upon the stretcher, there is no further handling of the patient until he is returned, upon the same stretcher, to his bed, all examinations being made through the stretcher, with the patient either recumbent or lying upon one side. I question, seriously, whether, in many of the cases studied, we subject the patient to as much strain as does the average clinician when he examines by routine physical methods.

Dr. Addinell Hewson: I show lantern slides of a case that occurred in my service at the Memorial Hospital, last March, of a young woman, aged nineteen years, brought in with a heavy bronchial cold, complaining of all the classical symptoms of appendicitis. It was found necessary to perform this operation at once; the anesthetic was given by a very careful person employed for that purpose and the operation was done through the sheath of the muscles of the abdomen without cutting any muscle at all. The patient was not exposed unduly and was taken back into the ward, and for two days afterward her temperature remained high. Under these circumstances the examination of the chest was made, and it was found that there was complete dulness on the right side, that the increased area of breath sounds on the left side was greatly increased and that the heart was pushed over to the right side. This gradually increased and with the increase of the mucous discharge from the bronchial tubes the patient would be relieved; then there would be an increase in the temperature again, the mucus would be more sticky, and it looked as if the lung was completely compressed through blocking of the bronchial tube upon that side. I had *x*-rays taken of this patient in varying lengths of time after the second day and show these so that the audience may see the exact condition of the patient. Copies of the twelve slides are deposited in the Mütter Museum, with a brief history of the patient at the time of the exposure to the *x*-ray.

Dr. Chevalier Jackson: I have not bronchoscoped a case of post-operative massive collapse of the lung. I do not know of anyone who has excepting Dr. Tucker, in this case, in which he collaborated with Dr. Lee. If, however, postoperative massive collapse of the lung is, as it certainly was in this case, obstructive atelectasis, then we have at the Bronchoscopic Clinic bronchoscoped hundreds of such cases; because obstructive atelectasis, like obstructive emphysema, is a relatively common occurrence in foreign-body cases, especially in the vegetable group. I think medical science is very greatly indebted to Dr. Lee for his initiative in asking for a bronchoscopy and local inspection of the interior of the bronchi. We have the internist who can tap, look and listen on the outside; we have the roentgenologist who can look through the patient; if we add to these the

bronchoscopist, who can look into the interior of the bronchi, we have a team which is bound to bring results in the study of pulmonary disease. In all spheres of medical activity wherever local methods of investigation have been developed things have been revolutionized, as you all know. In regard to collapse of the lung in diphtheria, as mentioned by Dr. Lee and first demonstrated by Dr. Pasteur, there was until recently a great paucity of literature, as Dr. Bowen stated of *x*-ray literature. Recently, however, bronchoscopy has been very extensively used in the study and treatment of tracheobronchial diphtheria. I am sorry to say municipal hospitals do not ordinarily have an equipment for raying every case of diphtheria, and in private practice it is often impracticable. Hence these cases are almost never rayed for diagnosis, but I have not the slightest doubt that collapse of the lung, or atelectasis, occurs in very many cases of diphtheria. Over and over again bronchoscopists have removed foreign-body plugs of diphtheritic membrane from bronchi which certainly were obstructed. While we do not have *x*-ray evidence to show that there was atelectasis of the tributary area, it is very logical to suppose that with a plugged bronchus absorption of air below it is followed by atelectasis in these diphtheritic cases. Emphasizing Dr. Bowen's remarks about collapse without pneumothorax, to get a conception of the mechanics of the matter we must consider the entire chest as one cavity with an exceedingly flexible partition, the mediastinum, that can move sidewise when there is a little plus pressure on one side or negative pressure on the other. This mobility of the mediastinum, I think, is perhaps not fully recognized. In conclusion, I should like to qualify the statement of Dr. Tucker, that there is practically no danger. As done by Dr. Tucker, without any anesthesia, general or local, there is practically no danger whatever in cases of obstructive atelectasis. If there are pathologic factors other than obstruction, there might be danger, especially in inexperienced hands; but bronchoscopists are accustomed to deal almost daily with obstructive atelectasis, even affecting part of both lungs; but there is practically little danger because we have the bronchoscopic tube down there for piping in air. Fletcher Ingals stated, years ago, that bronchoscopy for foreign body done by untrained men, who thought that all that was necessary in doing bronchoscopy was the possession of an instrument, was associated with at least 25 per cent mortality. If bronchoscopy is going to be done that way it is an exceedingly dangerous procedure; but done with a trained organization, by a man like Dr. Tucker, who is accustomed to working with one eye only through a long tube, there is no danger. By such as he, bronchoscopy can be done without any anesthesia, general or local, and it requires only a few minutes. I asked the patient just presented by Dr. Lee if the bronchoscopy hurt. He said: "No, it didn't; it gagged me a little." That kind of work means organization, teamwork, by men who have previously been trained to do bronchoscopy.

Dr. William P. Belk: One of the cases referred to by Dr. Lee was autopsied by me. Briefly, there was an abscess of about 3 cm. involving and occluding the bronchus to the lower lobe of the right lung. This lobe

was partially collapsed (about 50 per cent). From the pathological standpoint, this was undoubtedly a case of pulmonary collapse due to occlusion of a bronchus.

Dr. Edward E. Montgomery: I have been extremely interested in this paper. It brings back to my remembrance an article published in the *Medical Bulletin*, July, 1884, in which I reported 12 cases of tracheotomy for diphtheria, in 1 of which I had an opportunity to make an autopsy. All these patients had been treated for a length of time prior to the tracheotomy by tartar emetic and various emetic agents, with a view of dislodging the obstruction. In the patient on whom the autopsy was made there was a collapse of the upper half of both lungs. I notice, in all the descriptions given here of the *x*-ray findings, it is the lower portion of the lung they speak of as having collapsed; but in my patient the upper portion of the lungs was collapsed, perfectly white and pale; it was a condition which apparently accounted for the death of 10 others of these patients. I operated on 12 cases, of which but 1 recovered.

Dr. Simon S. Leopold: My experience with massive collapse dates back to 4 cases I saw at Camp Dix, and, curiously enough, they all occurred during a period of sixteen days, which made us think that for the cases we recognized there were many overlooked. We had the advantage of using a bedside portable *x*-ray apparatus. We noticed the same signs by *x*-ray as those described tonight.

I question the assertion that the displacement of the heart and mediastinum toward the affected side is due to so-called compensatory emphysema of the unaffected side, because, if that is true, it is hard to explain why the diaphragm on the affected side should rise and further encroach upon the pleural cavity. It would seem logical to agree with Lichtheim, who studied this in experimental animals, that there is created a vacuum on the affected side which allows the heart and mediastinum to be sucked over into this area of negative pressure. It seems that this is a better explanation, in view of the fact that the diaphragm is elevated.

In regard to the duration of the collapse attack, Dr. Gwyn cites a case in which the entire duration was six hours. In 1 case observed by me alternate collapse and recovery occurred three times in six days.

In regard to the anesthetic, it might be well to say that these cases follow local anesthesia as well as ether, and there is 1 case recorded in which it followed intraspinal stovain administration.

It is hard to understand why the postoperative cases are all unilateral. Bilateral collapse has been found at necropsy.

Dr. Manges, in discussing Dr. Holmes' paper, recently made the observation that the pathological process was an inflammation of the terminal bronchioles and their obstruction by a gelatinous secretion. The fact that all the postoperative cases had fever, and that all of them in which a leukocyte count was done showed a leukocytosis, indicates that in addition to the obstructive factor there must be infection. This view of Dr. Manges seems very appropriate since we have Dr. Tucker's beautiful illustration of the mechanism whereby this case was produced.

Dr. Willis F. Manges: This is an extremely interesting subject from the roentgen-ray point of view, certainly. I think the burden of the evidence tonight, in view of what Dr. Lee and Dr. Tucker have shown and in view of the case as shown by Dr. Hewson in which the condition recurred repeatedly, tends to indicate that there is a definite group of massive collapse due to plugging of the bronchus. The vast majority of these cases that I have seen, both in the literature and in practice, have shown involvement of the right lung, especially the lower, or lower and middle lobes. This is the location where foreign bodies are most commonly found. I have not seen an instance of collapse of an upper lobe without involvement of the lower lobe, following abdominal operation. The question as to whether it is an aspiration obstruction has not been made clear, but it probably does not play any very great part except that the anesthesia may influence the production of exudate in the bronchi following the operation and perhaps an excess of bronchial exudate during the anesthesia. I suspect that the bronchial plug, in the case reported by Drs. Lee and Tucker, was there as the result of exudate formed in the bronchus subsequent to the operation. Paralysis of the diaphragm I do not believe plays any part, or at least not any material part, in the mechanism of massive collapse except in so far as it might help to rid the lung or the bronchi of exudate. I think it is much more likely that paralysis of the cilia or of the muscles of the bronchi is responsible for the exudate remaining in the bronchus. I have certainly seen the diaphragm paralyzed from other causes without there being any sign of atelectasis or other pathology of the lung. The condition corresponds very much to a certain type of aspiration foreign body which at first does not completely plug a bronchus, but because of the irritant nature produces exudate distal to the foreign body, which may be very tenacious and extravasate into the smaller bronchi merely because it cannot go by the foreign body to be expelled. The exudate may even go into the air vesicles; but when the exudate completely plugs a bronchus and no more air gets in, there is then collapse of the lung distal to it because the air is absorbed. This condition was described by Dr. Jackson many years ago as "drowned lung." If the foreign body is removed soon after this takes place, Dr. Jackson can actually extract that secretion by suction and then the lung returns immediately to function. In other cases, where this exudate and collapse remain for days or weeks, it takes a longer time for the lung to return to normal, and, in fact, they behave just like the usual case of massive collapse following abdominal operation, shown in the literature. In the case shown by Drs. Lee and Tucker, function was promptly restored because the obstruction was removed early, before there was any chance for the exudate to organize. I believe that there is in these cases a definite element of pneumonitis—not a true lobar pneumonia, but an inflammation of both the bronchi and the parenchymal portion of the lung. I believe that the exudate from the inflammation of the bronchus is thick and tenacious and in excess of that which forms in the vesicular portions of the lung. In a case of massive collapse following abdominal operation which I have studied recently, the right diaphragm remains considerably higher

than normal, and there were small isolated areas of atelectasis throughout the right lower lobe for more than two months after the onset of the condition. There are still physical signs present, which show, I believe, that some of the smaller bronchial branches are still plugged with exudate or else that organization in the parenchymal portion of the lung occurred and prevents some of the vesicles from expanding.

Dr. Tucker (closing): We often see bronchial obstruction by secretion. In fact, as Dr. Manges and Dr. Pancoast, the consultant roentgenologists, and Dr. Kern, Dr. Carpenter, Dr. O. H. Perry Pepper, Dr. Miller and Dr. Gittings, the consultant internists, have noted in cases at the Bronchoscopic Clinic, one of the frequent problems is to determine whether, after removing a piece of peanut kernel, for instance, the development or persistence of obstruction in a portion of a lung was due to a plug of secretion or to additional and unremoved fragments of peanut kernel; in other words, to an aspirated foreign body or to an autogenous foreign body. In this case of Dr. Lee's there was what might be called an autogenous foreign body. I recall one case, in a child aged two years, seventeen life-saving bronchoscopies in four days were done, each time removing a plug of secretion that was occluding both main bronchial orifices at the bifurcation. In that case there was total abolition of the cough-reflex. This brings up the question of the cough-reflex and the possibility of its relation to these cases of massive collapse. Dr. Jackson has shown that after a foreign body, or even the bronchoscope itself, has remained unmoved in constant contact with the mucosa at one point in a bronchus, a condition of tolerance of fatigue is established and cough ceases so long as the foreign body remains unmoved. A foreign body knocking about keeps up frequent paroxysms of cough. It seems possible that the fixity of adherent masses of secretion diminishes the chances of bechic expulsion and favors accumulation to the point of complete occlusion. In this connection, also, may be considered Jackson's often-reiterated statement that "the cough-reflex is the watchdog of the lungs," and the accompanying advice not to drug the watchdog asleep. This brings up the question of the deep anesthesia required for abdominal surgery, with consequent prolonged abolition of the cough-reflex; and it also brings up the question of the preanesthetic or postanesthetic use of sedatives and antibechics, especially morphin. It would be interesting to have comparative statistics on patients operated upon with general and with local anesthesia, the latter without the use of morphin.

I have made no studies of the subject of massive collapse and have nothing to offer as to the etiologic factors; but through the courtesy of Dr. Walter Estelle Lee I have been able to see 2 cases of massive collapse, and, with the coöperation of Dr. Horace Williams, I have studied 1 case bronchoscopically at the Germantown Hospital. I am contributing only the clinical data in this one case of massive collapse, together with some of our observations on obstructive atelectasis in foreign-body cases that have been made in collaboration with Dr. Jackson, Dr. McCrae and Dr. Manges at the Bronchoscopic Clinics. As to the mechanism, pathology and

various clinical phases that have been so well presented by Dr. Lee, so far as I know, nothing more can be said. Dr. Manges has developed obstructive emphysema and obstructive atelectasis to a marvelous degree of accuracy as a means of roentgen-ray diagnosis of nonopaque foreign bodies. I should like to quote the roentgen-ray findings in a number of cases as evidence of the changes that take place in the lung in aspirated foreign-body cases.

The first case is one in which a lamp from a Whitehead mouth-gag lodged in the left bronchus. Dr. Sender reports that "the first film shows atelectasis of the left lung, with the heart displaced toward the affected side." It has been in this position for about two days. The second film was made ten minutes after removal of the foreign body. Dr. Sender reports: "There is still some slight degree of atelectasis and displacement, but the lung is beginning to fill with air."

In Case II a roentgen-ray film by Dr. Manges shows a pencil-cap in the left main bronchus and atelectasis of the left lung. The lung began clearing up immediately after removal of the pencil-cap, and an after-ray taken a few days later shows the lung entirely clear. The roentgen-ray findings in this case coincide with the physical findings of Dr. McCrae.

Case III is that of a dental root-canal reamer in the left upper-lobe bronchus. Here we have an illustration of inhibition in respiratory movements without collapse and without bronchial obstruction. It is interesting to note that the inhibition here altogether disappeared and respiratory movements were equal the next day after removal of the foreign body. Dr. McCrae was the first to observe this homolateral inhibition of movement in a case of nonobstructive foreign body.

Case IV, Dr. Manges' film of a patient with a peanut in the left main bronchus shows marked obstructive emphysema of the left lung, with displacement of the heart away from the affected side and downward displacement and flattening of the left diaphragm—shown best on expiration. The film, after removal of the foreign body, shows normal position of the heart and normal aëration of both lungs on inspiration and expiration.

Case V, a film by Dr. Pancoast, of a boy, aged two years, with a bean in the right main bronchus that had lodged in that position for forty-eight hours, shows complete atelectasis of the right lung with displacement of the heart and the mediastinum toward the affected side. The physical findings by Dr. Grier Miller, Dr. Howard Carpenter and Dr. J. Claxton Gittings coincided with the roentgen-ray findings of Dr. Pancoast. The second film shows complete clearing of the lung with the return of the heart and mediastinum to normal position twenty-four hours after the removal of the bean.

Case VI. The film is by Dr. Manges and shows an obstructive emphysema of the right lung due to the lodgment of a peanut in the right main bronchus, with displacement of the heart and mediastinum away from the affected side. On removal of the peanut bronchoscopically the obstructive emphysema disappeared and the heart returned to normal position.

Contrast this with Case VII. The film made by Dr. Pancoast shows

obstructive atelectasis due to lodgment of a bean in the right main bronchus, with the heart displaced toward the affected side. I removed the bean and within twenty-four hours the atelectasis had disappeared and the heart had gone back to its normal position.

Case VIII. The next four films, by Dr. Manges, are most remarkable because of the fact that we have atelectasis shifting from one lobe to another, and also atelectasis and obstructive emphysema existing at the same time in the same patient. The first films show obstructive atelectasis with the prune-stone blocking the right lower-lobe bronchus. The second films show the foreign body lodged in the right upper-lobe bronchus, with an atelectasis of the right upper lobe, obstructive emphysema of the right lower and middle lobes. Comparison of the films on inspiration and expiration demonstrates the presence of the obstructive emphysema.

Third films, made a few minutes after removal of the prune-seed, show that the obstructive emphysema has disappeared and the atelectasis has begun to clear, but there is still some displacement of the heart toward the affected side, showing remaining obstructive atelectasis.

The fourth films, made the day following the removal of the foreign body, show the lungs clear and the heart in normal position both on inspiration and expiration.

We are able to demonstrate bronchoscopically that the mechanism of obstructive emphysema depends upon the bronchial movements, the opening and lengthening on inspiration and the closing on expiration. In organic foreign bodies, particularly the peanut, with a flat surface, where there is marked inflammatory reaction at the site of lodgment, there is produced a valvelike action at this point with the trapping of air distal to the foreign body. This results in obstructive emphysema; but if the swelling increases to such an extent that this valve mechanism is lost, the bronchus becomes completely plugged on inspiration and expiration, and as a result the trapped air is absorbed and an obstructive atelectasis will occur. If there has been retention of secretions, purulent in character, the atelectasis will not be so marked, but we have instead the bronchial branches distal to the foreign body filled with secretion and "drowned lung" results. This may be accompanied by some degree of atelectasis, but there is not the marked displacement that is found where the drowning of the lung has not occurred.

In Dr. Lee's case of massive postoperative collapse, the film of the patient, by Dr. La Salle, shows an atelectasis of the right lower and middle lobes, with displacement of the heart toward the affected side, due to massive collapse of the lung occurring as a postoperative complication. On bronchoscopic examination, shortly after this film was made, we found some inflammatory reaction of the larynx and trachea, with thick, tenacious secretion in the trachea coming from the right main bronchus. The left bronchus was slightly inflammatory, but entirely clear of secretion. The right main bronchus shows a ring of thick, tenacious exudate completely surrounding the bronchial lumen. Air was entering the right upper lobe bronchus, but patches of this exudate were adherent to the bronchial walls at its orifice. The right stem bronchus was filled with this thick secretion, extending downward into the middle and lower lobe bronchi, completely

filling it. The secretion was aspirated from the stem bronchus, the middle-lobe bronchus and the right lower-lobe bronchus and its branches. The mucosa was reddened and slightly thickened, but not markedly edematous. The trachea and right bronchus were deviated toward the right, and it was noted that opening and closing excursions were very greatly lessened. There was no evidence of bronchial compression seen. Following bronchoscopy, air was heard to enter the lower and middle lobes quite freely, and the second film, taken immediately after bronchoscopy, shows increase of aëreation of the right middle and lower lobes, with less displacement of the heart than before bronchoscopy. The improvement was only temporary. The following day the physical examination showed that atelectasis had returned and the heart became displaced toward the affected side. This we felt was due to the reaccumulation of the thick secretion in the bronchi. The lungs cleared progressively, and the third film, made three days later, shows marked improvement in the atelectasis, with the heart returned almost to normal position. Bronchoscopic examination at this time showed some inflammatory condition of the tracheobronchial mucosa, with thin, mucopurulent secretion coming from the right main bronchus, but air was entering freely the upper-lobe, the middle-lobe and the lower-lobe bronchi. The deviation of the trachea and bronchi had disappeared, the opening and closing movements of the bronchus were normal. A swab, taken at the time of the first bronchoscopy, showed pure culture of the pneumococcus. I will be intensely interested in future bronchoscopy of similar cases. As to the danger of bronchoscopy, there is very little if the condition is purely of bronchial obstruction without any other complications. The matter of some coughing at the time of bronchoscopy, and its influence on a recently operated patient with abdominal drainage, is a question for the surgeon to decide in every case. No general anesthetic was given. Excessive cough was lessened by the administration of morphin, one hour before bronchoscopy.

# FEATURES OF THE SMALLPOX SITUATION IN PHILADELPHIA IN 1925*

By A. A. CAIRNS, M.D.

The history of smallpox occurring in Philadelphia during the past twenty-five years is as follows: From 1900 to 1904 inclusive there were 4941 cases and 894 deaths, making a death-rate of 18.09 per cent; from 1905 to 1924 inclusive there were 280 cases and 7 deaths, making a death-rate of 2.5 per cent. Practically 95 per cent of all patients were black.

In 1904 there were reported in Philadelphia 887 cases of smallpox, of which 867 cases were reported in the first six months of that year, and but 20 cases in the last six months of 1904.

In 1904 I took over the duties of the chief medical inspector, and during the first six months of that year there were over 260,000 persons vaccinated against smallpox under my personal supervision by block quarantine methods and vaccinations in industrial establishments. This work of vaccination checked the smallpox epidemic which had been raging in Philadelphia for four years. The same methods of regional quarantines have been continued to the present time.

From January 1 to June 30, 1925, there were reported 183 cases and 23 deaths, making a death-rate of 12.56 per cent. Of the 183 cases, 116 were primary and 67 secondary cases. The case-rate per 100,000 population was 9.25 per cent; death-rate per 100,000 population was 1.16 per cent: White race, 120 cases, 20 deaths; black race, 63 cases, 3 deaths.

From January 1, 1925, to June 30, 1925, practically 360 city blocks were quarantined. All persons living in those areas were examined by medical inspectors and those persons not giving a history of having been successfully vaccinated during the past five years or not showing satisfactory cicatrices were vaccinated.

* Read October 7, 1925.

In places of employment or other places frequented by smallpox patient, or direct contact with the individual suffering from the disease, every person was vaccinated irrespective of their previous vaccination. All direct contacts were vaccinated and held under quarantine for the full incubation period.

Approximately 200,000 were vaccinated by the Department of Public Health. Through other sources—physicians, hospitals, institutions, industrial plants, etc.—about 300,000 were vaccinated.

In a conference with the mayor and the president of council early in April of this year, regarding the increase in the number of cases of smallpox being reported at that time, I placed before these gentlemen that the working force of medical inspectors of the bureau of health was inadequate, and without question they authorized me to place on this work as many extra medical inspectors as would serve the purpose; the corps of medical inspectors was increased and we were able to divide the city in three section, placing each section under the charge of assistant diagnostician. This arrangement permitted the placing of three police quarantines at one time. This was done many mornings and covered practically the entire city.

The last case of smallpox was reported on June 11, 1925. The patient was an unvaccinated man who had been infected through a previous case.

A most regrettable occurrence of these 183 cases of smallpox we had in 1925 was a physician who attended a patient suffering with smallpox and who neglected to vaccinate himself, an unvaccinated four-year-old daughter of a physician, a medical student and a male nurse, all connected with the same institution.

On August 24, 1925, a case of smallpox was reported in a man infected in Denmark, South Carolina, before coming to Philadelphia; he had never been vaccinated.

During my tenure of office 2,000,000 of people have been vaccinated under my supervision. It is acknowledged that the regional quarantines and the vast number of vaccinations performed by this department have been factors in preventing several epidemics of smallpox in the past twenty years, and conviction is strong that Philadelphia would have suffered a more severe epidemic of the disease during 1925 had it not been for the quarantines and vaccinations.

I have no apologies to offer to the medical profession or the public

for the drastic quarantines, as it has been placed on my office to do the vaccinations of the City of Philadelphia, and had this not been carried out, as has been our custom, this city might have suffered inestimable damage. To place this responsibility on the health officer is expecting a great deal. For over twenty years I have been selling vaccinations to the residents of Philadelphia. If every infant were vaccinated before the first six months of life, and again at the age of puberty, smallpox would be an unknown disease; Philadelphia would not have had 183 cases of smallpox and 23 deaths from this disease, as we had during the first six months of this year.

There are some facts which cannot be too often repeated, and this is particularly true of those which relate to the value of vaccination against smallpox. It must be remembered that, in order to test this question and to settle it beyond dispute, it will be necessary to determine not how many among a given number of vaccinated persons contracted smallpox, but how many among a given number of those who were exposed to it were affected? It may be further added that it is not how many who have been vaccinated, but how many who have been thoroughly and properly vaccinated and exposed, who have fallen ill with smallpox?

For twenty years a mild type of smallpox was found in the cases reported in Philadelphia. The type of smallpox cases we have had during this year was a virulent type, many of them hemorrhagic, and a number of patients died within twenty-four hours after admission to the Philadelphia Hospital for Contagious Diseases. A high percentage of those who recovered from the disease were badly disfigured.

There were more smallpox cases in the United States last year than in any other country in the world. The number credited to this country is 55,528, against 46,374 for British India and 24,067 for European Russia. Of the American cases, 9425 were reported from California, where medical laws and health regulations must be in a bad way. Since so many cases are reported there, how long will it be until the rest of the United States is forced to regard that segment of the Pacific Coast as an incubator for smallpox?

For some years there has been a gradual letting down on the part of the health boards in the fundamentals of delaying with contagious disease. This has forced schools and colleges to insist that every

entering student be properly vaccinated and inoculated against these preventable diseases.

Those 55,528 cases of smallpox in America are so many reproaches to the health boards and the medical intelligence of the country.

*Paris Free of Smallpox.* Only 3 cases in year; due to vaccination, authorities say.

Smallpox has been virtually stamped out in Paris. Only 3 cases occurred during the last year, says a report to the Municipal Council, and these were all of a mild character. (Paris Sept. 25.) Freedom from the disease is attributed to insistence by health authorities upon vaccination. Every one of the 22,257 babies born in the maternity homes during the year was vaccinated, as well as 50,000 hospital patients and 48,000 children attending primary schools.

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## DISCUSSION

Dr. Alexander C. Abbott: I confess, Mr. President, to a great deal of humiliation when I read the world census of smallpox, as just quoted by Dr. Cairns, to find ourselves in the same category as European Russia. There is a manifest reason for the striking number of cases of smallpox in the United States, during the past few years, as compared to the civilizations of Western Europe. It is not that they know anything more about the prevention of smallpox than we do. It is merely that they employ the preventive measures more systematically and more conscientiously. We have at our fingers' ends all that is known of the one and only means for the prevention of smallpox, namely, vaccination. The explanation for our present position in the world census is indifference, ignorance and carelessness. There is working among us continuously and subtly and effectively a large group of defectives, mentally speaking, who are throwing every obstacle in the way of routine vaccination of the community. There is also a condition of inertia among us which, under the circumstances, is more or less natural. In one of the charts exhibited by Dr. Cairns we saw an interval of from eighteen to twenty years with almost no cases of the disease in this city. Under such circumstances it is only natural for both parents and physicians to grow a little careless on the matter of protective measures; in consequence, a new, unvaccinated generation is born and grows up. The question of vaccination becomes of secondary importance. The practitioner of medicine, who had been so careful to vaccinate every baby when we were threatened by an outbreak, became less eager to do so during the interval of exemption, with the result that there grew up large groups of unprotected individuals who may be compared to the tinder ready for the match.

For a number of years we have had smallpox all through the South, sometimes recognized, sometimes not, frequently of so mild a character that the patients were at large. Often the disease was so abnormal in its manifestations that it was not easily recognized. Many such cases occurred and are occurring among the laboring class who come to Philadelphia seeking employment in our mills and factories. While many such cases suffer little inconvenience themselves, yet they are infective for others, especially the unvaccinated, and are certainly accountable for outbreaks of the malady. These outbreaks begin in a mild form with many anomalous and abortive cases, but experience has shown that they gradually increase in severity until virulent smallpox is among us. I may be wrong, I hope I am, but in my judgment we are now facing a situation strongly analogous to that of 1897, which culminated, as Dr. Cairns has shown, in an epidemic that did not end until about 1904. We can prevent such a calamity only by unrelenting vigilance. We have no excuse for evading so plain a duty. We have in Pennsylvania excellent vaccination laws, perhaps no state has better, which provide for vaccination of the children in the public schools, and prohibit any other educational institution from accepting a student who does not give a certificate of successful vaccination. No one can matriculate at the University of Pennsylvania, at Jefferson College or at any other university or college in this state without such evidence. The new law in this particular is a very great improvement over the old. The old law provided only for school children, as that term is generally understood, and demanded only a certificate to the effect that the child "has been vaccinated." Many such certificates were worthless. I have seen hundreds—Dr. Cairns tells me he has seen many more—of school children's vaccination certificates signed by reputable physicians, stating that the holder of the certificate had been vaccinated, yet careful examination showed no sign of a successful vaccination. The operation was doubtless done and the certificate filled out and signed while the wound was drying, the doctor never having seen the child again and certifying only to the operation. The new law requires that the physician issue a certificate, not of the vaccination, but of a *successful* vaccination.

It is the accumulation of just such performances as these that accounts for many of the cases of recent years.

As Dr. Cairns pointed out, these outbreaks begin as mild, scattered cases, and each year a few severe cases, increasing in number, appear, until the character of the epidemic is unmistakable.

The prevention of smallpox is so easy and so certain that I incline to the opinion that any community in which the disease develops deserves all the inconvenience and expense coincident with an epidemic of a pestilential disease.

Dr. David H. Bergey: There is one phase of Dr. Cairn's paper that I think might be emphasized, and that is the large number of cases he found occurring in persons already vaccinated. It is true that the time elapsing between vaccination and attack is variable. We must remember that in protecting against smallpox, as far as our information goes, we are using as protective material not the actual virus of smallpox, but a modified

form of virus of smallpox which has always been regarded as affording protection for the time, but not indefinitely. We generally teach that persons should be vaccinated every five years, and I believe if we made a more general plea for revaccination at stated periods we could prevent most of the cases that have been included in those listed in the tables.

Dr. Cairns (closing): I felt that Dr. Woody would be present and perhaps would be in a better position to tell you about the smallpox cases in the Philadelphia Hospital for Contagious Diseases, where they are under his care and I see very few of them after they arrive in the hospital. When Dr. Abbott was Chief of the Bureau of Health the amount of money that was spent to control the smallpox epidemic in 1900–1904 was enormous. On two occasions the Director of Public Safety had half a million dollars given to him by Councils. That epidemic cost the city of Philadelphia several millions of dollars.

During the epidemic of 1925, in the absence of Dr. Krusen from the city, I called upon the Mayor, told him we required additional funds—I had been through one epidemic of smallpox and could not work without further appropriations. The Mayor unhesitatingly said we could have all the money necessary and the President of Council immediately gave $10,000, which later was increased to $30,000 in April. I appeared before them prior to recess in the summer and told them the fund was insufficient and $42,500 was appropriated. Today we are in position to return about $30,000.

Even with the small amount of money spent I feel we are throwing it away on a disease that is absolutely preventable. I do not know anything that is handled as carelessly as vaccination is today, and feel I am in better position to talk of that than any other physician in Philadelphia, the work is carelessly done and, as Dr. Abbott stated, the ordinary physician does not see a vaccination a second time. In 1904 about 10,000 children in the public schools and 1500 in the parochial schools held certificates of successful vaccination on file, and on personal examination of those children they were found not to have been successfully vaccinated. The children were personally vaccinated by me and successful vaccinations were obtained in 98 per cent.

I have been selling vaccination for the last twenty years and believe if the medical profession would insist on vaccinating infants born under their care before discharging the cases, and if all people were revaccinated, that smallpox would become an unknown disease. Jenner believed that once protected against smallpox, protected through life, but he had a proviso in that it must be *properly done*.

There was a great deal of experimenting in the technic of vaccinating the cases of smallpox contacts sent to the Philadelphia Hospital for Contagious Diseases in 1925 and who developed smallpox fifteen days after exposure. If there is anything in vaccination those people should have been protected. I believe the medical profession is experimenting. The technic I use in my teaching of vaccination is to make slight scarification, draw no blood and rub virus in, and I believe I can get 100 per cent of primary takes under these conditions.

# TRANSFER OF THE CUSTODIANSHIP OF THE COPLEY MEDAL PRESENTED TO WILLIAM HEWSON, F.R.S., IN 1768, BY THE ROYAL COLLEGE OF SURGEONS OF ENGLAND*

By ADDINELL HEWSON, Jr., M.D.

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In compliance to the President's request to give the result of my finding of anatomical specimens in a state of perfect preservation after one hundred and sixty years' preparation, I hesitate somewhat, owing to its being of such a personal family relative.

I was in search of Hunterian collections, where I knew William Hewson, F.R.S. (my greatgrandfather), would have been a contributor, as he was an associate of the Hunters in the Windmill School of London, England.

Therefore, on landing at Glasgow, I went to the University of Glasgow and, by the courtesy of the professor of anatomy and his assistant, saw catalogued, in part of the Hunterian collection, specimens of William Hewson's handiwork in mercurial and other injections in a magnificent state of preservation.

In the University of Edinburgh I knew I should not find any specimens (but asked, nevertheless), because of the dispute between Prof. Alexander Monro and William Hewson over the priority of the discovery of the lymphatics in the fish, in 1768 or a little before.

I did, however, find in the Comparative Anatomy Museum of the late Sir William Turner a donation from a Fellow of this College, the late Prof. William Smith Forbes, formerly professor of anatomy in Jefferson Medical College, of a skeleton of the American bison, beautifully prepared and mounted.

* Read October 7, 1925.

In London, at the Royal College of Surgeons, I was given an opportunity to examine seventy-two specimens of fine injections in various parts of the intestinal tube preserved in spirits, which permitted minute examination with blocks of glass $1\frac{1}{2}$ inches square by $\frac{1}{4}$ inch thick, over which had been stretched and dried injected mesenteries in perfect preservation.

I was given an opportunity to examine all the literature published by William Hewson and the Sydenham Society, together with Mary Stevenson Hewson's (his wife) letters, the original of which I had read in Philadelphia.

Photograph of Copley medal given to William Hewson, F.R.S., 1768.

There was a confirmation of a discovery I had made in my own dissecting-room work, viz., the best preparations were made by a neutral preservative solution. I was not aware that William Hewson had made this statement, but found it very clearly stated in the literature which Sir Arthur Keith placed at my disposal.

The solution now used with the best results to preserve the normal colors of the tissues of the body must be neutral.

I desire at this time to present to the College the autograph copies of the letters sent by William Hewson to Alexander Monro, to be kept among its precious archives, several pages of which have been photostated to permit examination by the Fellows.

I desire, also, to ask you, Mr. President, to receive for the College of Physicians of Philadelphia, as custodian, the Copley Medal

presented to William Hewson, in 1768, for the discovery of that year, by the Royal College of Surgeons of England. This medal to be the property of the oldest member of the family by the name of Hewson, under the will of Mary Stevenson Hewson, his widow, and since then passed to the oldest living member of the family. The depositor names Dr. William Hewson, his son, to succeed him, each succeeding owner to be named to the College at the time he assumes ownership on the death of his predecessor.

# THE GLANDULAR TREATMENT OF PITUITARY TUMORS AND HYPERPLASIAS*

By WALTER TIMME, M.D.
NEW YORK

In order that a more or less rational treatment may be devised for the various types of pathological enlargements of the pituitary body, it is, of course, quite necessary to classify these disorders. Such classification, however, is difficult, for we have little basis for it short of the comparatively few autopsies and the reports of the pathological tissues removed at operation. It has been heretofore simply a matter of determining whether a mass, either of or about the hypophysis, existed, that gave pressure or metabolic symptoms, or both. If determined in the negative, then no operative interference was undertaken; if in the affirmative, then surgery was evoked for relief. But the surgical results were not of such a nature as to call forth unbounded confidence from the prospective patient, and so surgery, except in the most extreme cases, was frequently refused. These patients, then, turned for relief to nonsurgical methods. And so it happened that therapeutic attacks were made upon the disease processes on the barest conceivable theoretical grounds without any but the merest hope of a chance of success. And in almost all these cases the condition became progressively worse and terminated fatally. Then came a series of cases reported since 1912 by Waldeck (1912), Clothier and Dewitte, Reber (1915), Elsberg, Krug, de Schweinitz and myself (1916), in which the treatment that led to a successful issue was either pituitary substance administered by mouth or pituitrin hypodermatically or both, together with occasional doses of thyroid. In these cases there resulted not only amelioration of the symptoms but apparent actual cure. Indeed, in my case, the outstanding features of nausea or vomiting, beginning acromegaly, intense headache,

* Read October 7, 1925.

bitemporal diminution of the visual fields, sugar metabolic disturbances and enlargement of the sella turcica had left no choice in the matter of diagnosis, and operation was only deferred because of incidental reasons. On glandular treatment, undertaken because of the necessity of relieving her intense headaches, the headaches disappeared, the visual fields became again normal, the other symptoms receded and the patient is today, some ten years later, completely well, married and the mother of several children. The treatment in this, my first case, consisted in the administration of whole-gland pituitary substance, varying from 0.5 to 3 grains per day; injections of pituitrin for two or three days a week; and later, thyroid, 0.5 to 1 grain, once daily. For one or two weeks a month, 2 grains of lutein, was likewise administered as her menses had become much delayed. They returned to normal as the improvement in other symptoms came on.

The same treatment applied to other cases of probable pituitary neoplasm, giving the same or similar symptoms, curiously had no effect whatever upon the growth or upon the symptoms. Apparently there must be some difference in the nature of the tumor mass in these cases that causes such critical differences in their reactions to the same therapeutic attack. It is just at this point that the necessity arises for a proper classification, so that the cases that may be benefited by treatment may at once be separated from those necessitating surgery. Let us go into this matter at once. From a study of some 20 cases in the course of the last ten years, in which the diagnosis of pituitary tumor varied from doubtful to certain and in which glandular treatment was eminently successful as compared with a rather large number in which failure attended a therapeutic attack, there have been certain similarities strikingly evident in the successful ones. *In each of these cases the pituitary* disturbance followed, either (1) some other glandular difficulties, such as castration, puberty, menopause, ovariectomy; (2) arose in those cases that have been described by me as belonging to the compensatory syndrome group, namely, those in which the pituitary gland presumably becomes hyperplasic in order to compensate for the deficiencies superinduced by a status hypoplasticus with deficient adrenals, which cases have the earmarks of status thymicolymphaticus or, (3) developed in a group formed by those patients residing in goiter regions. The inactivity of the thryoid in these produces again a compensatory enlargement of the pituitary with

all the signs, metabolic and pressure that *bona fide* pituitary tumors produce. Not to bore you too long with case recitals, I still must crave your indulgence at this point to cite rapidly the most interesting and suggestive types representative of these 3 groups.

Group I.—Several examples of pituitary disturbance, following upon hysterectomy as it was practised fifteen to twenty years ago for many minor complaints—the so-called hysteria among others—giving many symptoms of neoplasm, recur to my mind. Interesting in this connection is one case operated by Lawson Tait, which developed the headache, the acromegaly and some contraction of the fields many years after the abdominal operation, in fact, at the time the normal menopause would have arrived. This case, as are all those that follow ovarian disturbances, is much benefited by various forms of ovarian glandular products in addition to pituitary medication. Destruction or ablation of the testicles may occasionally likewise produce an enlargement of the pituitary resembling a neoplasm. While these cases do not succumb to testicular glandular therapy, yet the administration of pituitary extract and pituitrin usually will keep the hyperplasia in check.

Group II.—The second group of pituitary disturbance simulating neoplasm is that in which the pituitary becomes hyperplasic in the course of compensation for status hypoplasticus. These cases are frequently found to have large and persistent thymus glands, small cardiovascular systems and small adrenals. They develop the intratemporal headache of pituitary disease, a large and eroded sella, giantism, occasionally mild degrees of choked disc and contraction of the fields. The treatment of these cases, as outlined by me elsewhere, consists in the administration of small doses of iodide, thyroid and pituitary substance (a combination of 1 to 4 grains of the anterior lobe and 0.1 to 1 grain of the whole gland). The pituitary medication *per os* in order to be effective, in my experience at least, ought to be given at least two hours after meals. Pituitrin, which may be used in conjunction with feeding of the glandular product, has many disadvantages when given hypodermatically. It causes at first intense pallor and prostration with syncope and, if given over long periods of time, marked asthenia. In the past two years we have been giving it in drop doses by nostril in a medicine dropper, or in the retropharyngeal space with throat application. Excellent results are obtained by this method, even in those cases with the intense polyuria of diabetes insipidus.

Group III.—One patient of this group truly representative, and of intense interest from several glandular standpoints, a woman, aged forty-two years, highly intelligent, living in Central New York State—a goiter region—began to complain in 1918 of intense headaches, intratemporal in character, accompanied later by nausea and vomiting, a gradually increasing adiposity, lethargy, confusion of thought, loss of memory and progressive loss of vision. Her visual fields, examined at the Cornell Clinic at Ithaca, were found bitem-

porally hemiopic, the sella turcica enlarged and eroded and there seemed only one solution to the situation. These examinations were not all made at one time, but over the course of two or more years. The condition in this time became progressively worse. Dr. Martin Tinker, of Ithaca, had been asked to see the case in view of an impending sellar decompression, and, not entirely satisfied to do the operation without first giving the patient the benefit of glandular therapy, referred the case. Our examination confirmed practically all his findings, and in addition we determined the basic metabolic rate, which was found variable, from + 20 per cent to + 5 per cent. The patient had a slightly enlarged thyroid struma of rather boggy consistency. A skin-reaction line could not be elicited and her subcutaneous tissue gave one the impression of a mild myxedema. To us the case seemed clinically to be both hypothyroid and pituitary in its aspects, and our treatment began with the administration of small doses of sodium iodide and of thyroid in spite of the high metabolic rate. In a few weeks the headaches disappeared, the myxedematous appearance vanished, the patient lost weight, her mental confusion lessened markedly, the nausea and vomiting ceased altogether and the visual fields gradually improved. The basal metabolic rate became *reduced* to − 5 per cent, and this on thyroid medication—a direct contradiction to the accepted doctrine of the relationship of thyroid activity to basal metabolism. After a few weeks, whole-gland pituitary substance, grain $\frac{1}{4}$, twice daily, was added to the other medication and pituitrin was occasionally given hypodermatically, but produced such asthenia that it was discontinued. On varying dosages of these three medicaments the patient made a complete recovery, so that today she is well in every respect, even including her visual fields. Of great interest is the added fact that one of her children was beginning to show a pituitary condition, which succumbed to the mere administration of iodine. The interpretation of this case, of course, would be that the pituitary symptoms were produced by a compensatory enlargement—hyperplasia—due to thyroid deficiency, giving all the signs of pressure produced by a neoplasm. The basal metabolic rate is interesting, as it does not conform to the usual low rate of the myxedematous patient. Perhaps it was kept above the normal level by an overactive pituitary; at any rate, the case is a classical example of the vagaries that may be produced in the course of an iodine deficiency. Furthermore, the *reduction* of the metabolic rate by thyroid administration is, against all rules, thought to be established in this domain. The possible criticism, that there was error in the performance of the tests, is negatived by the fact that the many determinations that were made were in different cities in different laboratories by different technicians, and were all within reasonable closeness of result. To put it succinctly, a patient coming from a goiter region, with myxedema complicated with pituitary hyperplasia, gave a high basal metabolic rate which was lowered by thyroid and iodide medication—a paradox.

These three types of hyperplasia of the pituitary gland, then, represent the groups that may be markedly helped and even entirely

cured of their complaints by glandular medication. As each of these groups represents a pituitary mass which in every respect may produce the symptomatology of a true pituitary neoplasm, from metabolic nuances to the gravest of pressure symptoms, it is advisable that they be thoroughly studied and understood as their differential diagnosis from neoplasm may save many an operative hazard. Occasionally, so-called benign adenomata arise in these hyperplasic tissues, and then there is no sharp line of demarcation between hyperplasia and tumor formation. True neoplastic growths of the pituitary, or in its neighborhood, can no more be influenced by glandular therapy than they can elsewhere in the body. The three important criteria, then, that serve to distinguish these cases having pituitary masses amenable to glandular therapeutic attack from those with true neoplastic growth are:

1. Previous operative or other critical disturbances of the gonads.
2. Status thymico-lymphaticus preceding the pituitary symptoms.
3. Long-standing thyroid insufficiency, especially as found in the goiter belt with lack of iodine.

Perhaps, as is more than likely, this grouping will be found to be inadequate or to need much qualification. It is but a crude beginning toward a nicer discrimination of pituitary enlargements.

When we come to the minor disturbances of the pituitary with enlargement of the hypophysis—whose number is legion and whose diagnosis on a pathological basis rather than upon a clinical one is of the utmost difficulty, especially since the epoch-making experiments of Camus and Roussy—we are confounded with the paradox, at times, of a pituitary glandular therapy being specific against disturbances not of pituitary origin: Witness the effect of pituitrin upon diabetes insipidus. And yet, the Continental School, represented by the Germans and Austrians, as we might suppose, opposes the interpretation offered upon their experiments by Camus and Roussy. We need not go into the merits of the controversy at the present time, as our theme is not diagnosis *per se*, but of therapeutic attack. And if you will permit me, I will go into the treatment of but one more of the many disturbances credited to pituitary malfunction due to hyperplasia, but one which is omnipresent and ubiquitous. This is the headache of pituitary origin, and I mention it in this paper only because, while it is often the precursor of pituitary hyperplasia or neoplasm, yet frequently it forms an entity appar-

ently of its own, with recurrent attacks following intervals of complete freedom.

Pituitary headaches, with their characteristic location, their frequent occurrence with eye-muscle and visual disturbances, their prostrating character and their inaccessibility to attack by our fraternity, are fruitful fields for therapeutic glandular attack. A few diagnostic criteria may here be necessary to indicate the kind of headache which is pituitary in character and which lends itself to our therapeutic management:

The patient complains of the headache as a pain *within* the head, not of compression, of a boring or bursting or throbbing character, and movements of the head are accompanied by a subjective sensation of a mass within the head moving in the same direction. The locus of pain is variously described as "between the temples," below the crown, back of the eyes or midway between the bridge of the nose and the occiput—all lines converging to the sella turcica. These headaches come on after undue fatigue, after fasting, during or before menstrual periods, after meals rich in carbohydrate food, after long-continued depression or chagrin, after undue sexual intercourse and many other less notable causes. Occasionally, accompanying the headache, are oculomotor disturbances with visual symptoms. These are probably due to interference by the enlarging pituitary body upon the cavernous sinus and its nerves, the third and fourth, ophthalmic division of the fifth cranial trunks leading to unilateral or bilateral ptosis, strabismus with diplopia and the other oculomotor disturbances.

Radiographs of the skull show erosion of the clinoid processes of the sella or else an extremely small sella apparently enclosed or bridged by long processes. Left to themselves these headaches persist for several decades, coming on periodically or else after the intercurrent causes mentioned above. The sella gradually enlarges through the recurrent hyperplasic attacks which are connoted by the headaches until a moderate enlargement of the gland can take place without undue pressure and then the headaches spontaneously cease. Interesting to note is the fact that these headaches are often only the indicators of a compensatory process during the course of which the pituitary becomes enlarged and overactive—and are then found in the same three groups of cases which have been described above in classifying pituitary hyperplasias amenable to therapy.

The therapy applicable to them is specific, namely, the administration of whole-gland pituitary substance in very small doses, from $\frac{1}{10}$ to $\frac{1}{4}$ grain once or twice daily, at least two hours after meals. Every fourth or fifth day the administration should be omitted. If too much extract is given the headaches are made worse or even may be brought on thereby. Should they be accompanied by mild hyperthyroid states, with low-grade excitement and irritability, then it is an excellent plan to give, in addition to the pituitary extract, hypodermatic injections of cacodylate of soda, from $\frac{3}{4}$ to $1\frac{1}{2}$ grains every alternate day for 15 to 20 injections. An important point in the treatment is to discontinue the pituitary extract as soon as the premonitory signs of a headache make their appearance and not begin again until the headache has disappeared. Of the various exciting causes mentioned above, those that are remedial should be remedied, such as going without food too long or indulging in too much carbohydrate food. By these simple means many so-called chronic migrainous attacks of pituitary origin may be reduced to two or three yearly, or even made to disappear entirely.

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## DISCUSSION

Dr. Francis X. Dercum: The paper to which we have just listened is of practical value. There are some cases in which surgical interference is not indicated or in which surgical interference may be declined. In such cases a trial should be made of organotherapy. The questions raised by the author of the paper deal largely with endocrine imbalances. Dr. Timme has referred repeatedly to the status hypoplasticus or the status thymicolymphaticus, as we frequently speak of it. It would seem that in this state the mesoderm or mesenchyme of the embryo persists to an undue degree. In it differentiation does not take place as rapidly as in the tissues of the other layers; it does not proceed to the same high level. Muscle, bone, gland cell, nerve cell, heart and vessels are not formed from it as readily as they should, neither in kind nor in amount, and as a result we have an excess of this primitive lymphoid tissue persisting. Very curiously, this lymphoid tissue in large degree masses itself, among other things, about the thymus. It almost seems that the epithelial portion of the thymus forms a special nidus which attracts the lymphocytes and that it furnishes a substance especially favorable to lymphocyte life. Now in the status thymicolymphaticus there is a definite imbalance and especially a lowering of the metabolism of the organism. Under the circumstances the thyroid gland responds to the imbalance, responds to the lowered metabolism, by an increased functional activity. This may lead, and very frequently

does, to an excessive activity of the thyroid gland and to various degrees of hyperthyroidism up to a fully-developed exophthalmic goiter. In given instances the pituitary gland also partakes of the imbalance and likewise becomes enlarged. It would appear that, as in the case of the thyroid, the pituitary is in direct relation with the thymus. In extirpation of the thyroid in animals the anterior lobe of the pituitary enlarges, but in extirpation of the anterior lobe of the pituitary the thyroid remains unaffected. In other words, the pituitary gland is primarily related to the thymus and in the status thymicolymphaticus may respond by enlarging, just as does the thyroid. Further, quite frequently both glands enlarge at the same time. It is quite a common experience, for instance, to find that when an exophthalmic goiter makes its appearance in youth that the patient is also unusually tall and presents other evidences of pituitary overactivity. Again, when the thyroid for some reason fails to respond or responds inadequately the hyperpituitarism may go on to a more or less pronounced acromegaly.

In regard to the headaches which may be met with in mild cases of pituitary enlargement and which suggest migraine, much can often be accomplished by the administration of thyroid substance. Naturally, if metabolism be stimulated by thyroid administration, the pituitary is called upon to do less, and it is readily conceivable, if enlarged, may grow smaller in volume. Among these are the adipose cases that we meet with in which there are evidences of thyroid and other endocrine deficiencies and inadequacies.

The relation of the pituitary to the gonads is, of course, a very old story. It is, however, particularly in cases of pronounced hypopituitarism such as we meet with in dystrophia adiposogenitalis (Froelich's disease) that endocrine therapy conspicuously fails, possibly because of the malignancy that has already been established in the pituitary tumor. In regard to the administration of pituitary substance for so-called pituitary headache, I have never myself observed any definite result unless the administration was accompanied by thyroid, and I have always attributed the results to the thyroid.

Dr. Charles H. Frazier: It seems almost like carrying coals to Newcastle to attempt to make any addition to the contribution of Dr. Timme on endocrine disturbances, so large has been his experience. Of course, the surgeon's experience differs essentially from that of the endocrinologist. The surgeon, that is the neurosurgeon, sees in his clinic only those patients in whom endocrinology has been tried and failed. I think in our entire series we have had but 1 or 2 cases where we thought glandular feeding was of the slightest benefit. On the pituitary register in the Neurosurgical Clinic of the University Hospital there are now some 185 cases, and of this number 102 have been adenomata. In this group it is rather interesting to note that—despite the fact there is considerable constancy as to the size of the tumor and its anatomic relationship, as it always takes its origin from the anterior lobe—there is the greatest variation in the clinical expression: in some, dwarfism; in some, acromegaly; in

others, the Froelich syndrome; in some, a combination of the two. In others there may be no evidence whatsoever of pituitary stigmata—in practically half of our adenomata series was this the case.

Now, with regard to the management and treatment of pituitary lesions, my experience differs from that of Dr. Timme. Dr. Timme says he never had to send a case to the surgeon. I say in every case referred to me, we have never been able to relieve the patient by feeding glandular extracts. So it would seem as though we were as far apart as the poles. But I think I could convince Dr. Timme if he would stay here long enough to make rounds with me: I would show him how many patients with pituitary disease are in desperate condition, with rapidly failing vision, usually already blind in one eye; many suffering, yes, incapacitated, because of the intense bitemporal headache. Something must be done, and immediately, to relieve the pressure phenomena, and usually this something is an operation. In a few cases, perhaps 5 per cent, we have used radiation with gratifying results. Headaches have disappeared, menses have been reëstablished and vision restored. So in cases which are not urgent, when optic atrophy is not far advanced and vision not threatened, the effect of radiation should be tried, providing the patient can be kept under the supervision of a competent ophthalmologist who can determine with the perimeter whether the lesion is stationary or retrogressing, and providing that from time to time the measurements of the sella turcica may be determined. In 3 or 4 per cent of our 102 cases there was a decided and satisfactory result following radiation. All of these were of comparatively recent origin. The vast majority of cases that find their way into our clinic are cases of long standing, of ten, fifteen or twenty-five years' duration. It is rather hopeless under these circumstances to expect to improve them by anything but surgical treatment.

It may be out of place here to discuss technic, but I should like merely to state what our plan of procedure is: Whenever we have a primary pituitary lesion, such as the adenomata we are discussing, it is our practice to perform a subcapsular evacuation by the transphenoidal approach. We prefer this operation to the transfrontal method, urged by others, because of its greater safety. It eliminates many hazards and risks of the other procedure. Our mortality now is about 3 per cent and is getting lower and lower all the time. We have lost but 1 case since 1919. By this procedure we have been able not only to relieve the pressure phenomena and thereby improve or restore vision, but we have observed a beneficial effect upon pituitary dysfunction. We had not anticipated this. In some cases menses have been reëstablished; in some instances fatiguability has given way to normal vigor; in some the patient is able to wear a smaller glove and shoe.

I should like to ask Dr. Timme what the effect of organotherapy may be upon the histology of an adenoma, also whether he has observed in the polyglandular types that the effect of hyperthyroidism and of hyperpituitarism upon basal metabolism offset one another. In one of my patients, an exaggerated case of exophthalmic goiter associated with pituitary disorder, the metabolic rate was within normal limits. Would

the tendency of an elevated metabolism rate, as in exophthalmic goiter, be offset by the tendency for a minus metabolic rate in a pituitary disorder?

Dr. George E. de Schweinitz: It may be interesting to refer for a moment to the effect on the pituitary gland of the elimination of the ovaries and testicles, on which subject there is, as Dr. Dercum has said, considerable experimental evidence.

For instance, W. H. F. Addison has, among other investigators, described the elaborate cell changes in the hypophysis of the albino rat after castration. Moreover, he has noted that the reaction in cells of the hypophysis after removal of the ovaries follows the same general course as does the reaction in the hypophysis of castrated male animals.

In preparation of the Bowman lecture (1923), with the assistance of Dr. Alexander Fewell and the coöperation of Drs. John Clark and Charles Norris, I endeavored to ascertain whether the visual fields of women after double oöphorectomy would exhibit depressions indicative of pituitary gland disorder similar to those which are not uncommonly found during the later stages of pregnancy, due apparently to temporary enlargement of the gland. We found in 6 women, whose eyes were normal, three, four, five, six, seven and twelve months respectively after operation, no strictly normal fields, and in 3 of them field defects suggestive of those which have been charted as indicating the first stage of an advancing bitemporal hemianopsia, the result of chiasmal involvement in association with pituitary struma or enlargement, but none of the patients exhibited any general signs of pituitary dysfunction. The number of patients is much too small to justify any definite conclusions, but the results indicate the need of a much more comprehensive research along these lines.

Referring now more exactly to the subject of Dr. Timme's paper, this may be said: The difficulty of reaching a decision as to which types of pituitary dysfunction are amenable to glandular feeding is well recognized. Hence we are indebted to the essayist of the evening, whose characteristically excellent address has clarified the therapeutic atmosphere. Quite ready to show deference to the pessimism with which organotherapy in pituitary disorders is regarded by a number of distinguished surgeons and neurologists, readily admitting that the physician must be slow to draw conclusions from the apparent effect of glandular extract given by the mouth, recognizing that a number of "cures" of hypophyseal disorders are due, not to the remedies administered but to spontaneous decompression or to the rupture of a cyst of the pituitary body, it is impossible to escape the conviction, based on the examination of the literature and on personal observation, that in certain circumstances glandular feeding has established a therapeutic value.

It is, I think, generally admitted that this medicinal regimen possesses a definite value in the treatment of girls who (to quote from my Bowman lecture) exhibit transitory pituitary body symptoms during early adolescence. Prior to the age of puberty or, more exactly, prior to its tardy establishment, headaches appear, unrelieved by the usual measures; men-

struation is delayed from two to three years beyond the ordinary time of its appearance and during this period growth is abnormally rapid, although not excessive, with gain in weight and deposition of fat, resulting in an ungainly figure; headache increases in severity, the pain being frontal, that is, intratemporal; asthenopia is persistent; mentality childish or poorly developed; when the menses appear they are scanty and irregular. General treatment is ineffectual, but surprising improvement takes place under the influence of pituitary body feeding.

This type has been studied especially by Dr. Walter R. Parker and is familiar to all of us. Parker found no peripheral field defects essentially indicative of enlargement of the pituitary body, but relative exactly central scotomas were discovered, suggesting axial fiber involvement. In this respect a difference from the fields in pregnancy and those occasionally noted in some patients during menstruation is evident. But in this early adolescent type nerve-head changes (congestion) are present, which are absent in the pregnant patients. If the former depends upon a temporary disorder of the pituitary body (and the general symptoms indicate that this disorder does exist) they (the pituitary changes) must possess a character which differs from that which is normal to pregnancy.

The thought naturally occurs that a toxin is elaborated which affects the optic nerve (which is ophthalmoscopically congested), and that the scotomas depend upon an axial fiber involvement, similar to that which arises under the influence of other toxic influences. Visual field studies, according to the newer methods, are much to be desired in this form of early temporary adolescent dyspituitarism.

We stand on a far less certain therapeutic ground in the presence of those patients who exhibit the indications of gross hypophyseal disorder, and yet rather startling recoveries have been recorded. I have placed on record the case histories of 3 such patients, to which Dr. Timme has referred. In 1 of these patients who passed through all the stages of an advancing bitemporal hemianopsia to temporary loss of vision, the restoration of sight was complete after a prolonged administration of thyroid extract, and for a time mercury, the patient is not a syphilitic. It is, however, not certain whether this startlingly good result was due to the remedy or to a spontaneous decompression. In another patient an almost exactly similar restoration of vision was apparently due to the effect of combined thyroid and pituitary body extracts. Both of these patients are entirely well now, years after the beginning of their visual trouble. One of these patients (the first one mentioned) has had two relapses; in each instance a renewal of the glandular feeding brought about a restoration of the vision. In 2 other patients the effect of organotherapy was good, but not so perfect as in those just mentioned; also these patients have disappeared from observation.

Not very infrequently one encounters patients with visual and other signs of pituitary disease where glandular feeding materially modifies the headache or entirely dissipates it, but has no influence on the defective fields or general symptoms.

The employment of organotherapy after operation, in the hopes of prolonging the good results or of preventing a relapse of symptoms, has, I think, been largely discontinued since the advantages of radiation (*x*-rays and radiation) have been appreciated.

Doubtless greater care in securing satisfactory gland preparations might improve our therapeutic results, and we are indebted to Dr. Timme for a description of his technic in this respect.

Dr. Timme (closing): I would like to thank the gentlemen who discussed my paper for their very able and thorough discussion and for the points they brought out. I wish to take up several of them now and answer them, if I can.

Dr. Dercum made the just remark that a great many of the cases that we see that are called migraine are not migraine at all, but are pituitary disturbances. I should go even a little further and say that *most* of the so-called cases we see are pituitary disturbances and very few of them are what we are pleased to term of toxic origin. If we examine carefully—as we do—every case of headache with an *x*-ray of the skull and a thorough biochemical examination we would be surprised to see how very often there is evidence of enlargement of the pituitary body.

Dr. Frazier asks some questions which are difficult to answer. For instance, in the first place, he asks whether feeding glandular products perhaps changes the histologic character of the pituitary growth. I do not know, because our cases do not die, so that we cannot examine the character of the growth. I do know that feeding iodin changes the histologic character of the thyroid gland. I presume on the same basis it probably does change the pituitary histology. Then as regards the balancing of basal metabolic rates. Dr. Frazier is absolutely on solid ground there—he thinks as I do! There is no doubt that we are making too much use of the laboratory, and especially use of the basal metabolic tests, in the wrong way. It is very simple to have basal metabolic tests done, but as to their interpretation, you will find that other elements than the thyroid enter, similar to the case I mentioned, in which there was a so-called paradoxical lower rate following the administration of iodin. Dr. Frazier says the cases that come to him do so on account of the pressure symptoms of an increasingly large pituitary body. I think we are agreed on that. The cases we see that show dystrophies, or Dercum's syndrome, show sella turcica changes that are not at all constant, sometimes with enormously enlarged cavities and occasionally with contracted ones. Is it an increase in the secretion of the pituitary that produces the metabolic changes, or is it a faulty secretion? I agree thoroughly with Dr. Frazier that the large pituitaries we see are not necessarily those producing metabolic disturbances.

Dr. de Schweinitz mentioned his experience with fat adolescent girls that show their stigmata of pituitary disturbance in that they have pituitary headaches which come on two or three days before a menstrual period. They may also follow gorging of carbohydrate food. Treatment of these

girls by pituitary substance is extremely helpful. The paracentral scotomata of which Dr. de Schweinitz speaks are probably not found except by expert examination. Nevertheless, while they have no gross visual disturbances, they have circulatory disturbances. The fundus of the eye shows often large, engorged veins with narrow arteries and occasionally one finds in these cases with a so-called migraine attack ptosis of one lid, diplopia, or other oculomotor disturbance due to the pressure of the occasionally enlarged pituitary upon the cavernous sinus with its accompanying cranial nerves, the third, fourth and ophthalmic division of the fifth. I thank you for the courtesy you so kindly extended to me to lay my views before you.

# CERTAIN EXPERIENCES WITH GALL-BLADDER SURGERY*

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The literature upon gall-bladder disease and gall stones is of huge proportions and this communication may have little to merit its publication. But we often note that conclusions and figures of a decade or more ago are used to support opinions of the present day and do not represent current surgical practice. This paper is based on an experience comprising 128 operations for chronic gall-bladder and tract disease, including gall stones, operated upon in the hospital of the University of Pennsylvania and the Misericordia Hospital from September 1, 1922, to May 1, 1925, and represents my entire experience during this time.

Next to appendicitis, disease of the extrahepatic ducts and gall bladder is the most frequent of the lesions treated by the surgeon. Because of the relation to the liver and pancreas, they are much more interesting and very much more complicated than acute or chronic disease of the appendix. The great increase of interest in the function of the liver and of the gall bladder and the minute studies of the pathology of the gall bladder and the chemistry of the bile have been watched with great interest by surgeons, every ready to apply the work of the laboratory to the solution of clinical problems.

The diagnosis of gall-bladder disease is not particularly difficult if we keep certain facts in mind. Most cases occur in stout women who have borne children. In the series reported in this paper 82.5 per cent were women. I have noted that most of these women have put on weight rather rapidly, many have developed the early symptoms shortly after the birth of a child. The ages varied from

* Read November 4, 1925.

nineteen to seventy-six years and averaged forty-three years; 59 per cent of the patients were over forty and 12 per cent were over sixty years of age. This means the age when the patients came to operation and not the age at the onset of symptoms, which I have not calculated. It is interesting to recall that Alvarez[1] believes that on the average, nearly twenty years elapses between onset and operation, a period characterized by many courses of treatment, most of them directed against such vague disorders as nervous indigestion, flatulent dyspepsia, intestinal autointoxication and the like. The attacks are usually sudden in onset and short in duration and are not amenable to dietary regulation.

Many patients complain of mild symptoms, suggesting a focal infection, such as chilliness, vague pains, joint pains, etc. During the attack the liver edge is nearly always tender. Sometime later the attacks become more severe and often typical of acute cholecystitis. Colic occurs and the tender, distended gall bladder can be palpated. Usually these attacks extend over many years and are rarely severe enough to require an anodyne. Flatulence, epigastric distress, eructations and slight nausea may accompany the taking of food.

If we will remember that next to appendicitis, gall-bladder disease is the most frequent surgical lesion in the abdomen, that it is not necessary to wait for typical violent colic and never for jaundice, we will save lives and most postoperative suffering. In the series herein reported every chronic uncomplicated case recovered. Empyema, common duct stone, biliary cirrhosis and pancreatitis are the major complications. Extensive adhesions from frequent acute attacks prevent the complete recovery of the patient after cholecystectomy.

In recent years we have learned to lean heavily on the laboratory for assistance in diagnosis. A simple gastric analysis is not of much value, but it is well to know that the values are low in gall-bladder dyspepsia, whereas in duodenal ulcer they are almost invariably high. Gatewood[2] found a chlorhydria or hypoacidity in 45 per cent of a series of 192 patients will gall-stone disease.

The *x*-ray often helps materially in the diagnosis of pericholecystic adhesions. "Spider-leg" distortion may be seen, but is also present in the congenital membrane case; high fixation of the duodenum, fixation of the hepatic flexure, distortion of the pylorus to the right are all significant. The direct evidence is not so important unless

positive. Thirty-one of my patients were *x*-rayed for stones: In 9 cases stones were diagnosed and in 8 the finding was correct (89 per cent); in 19 cases the *x*-ray evidence was negative, but in only 5 were gall stones absent and the *x*-ray correct (26 per cent). In the other 3 the finding was simply a "visible gall bladder;" 2 had stones and 1 did not. Very recently we have had added to our resources the Graham test (cholecystography). It is not necessary to discuss this test, as the literature now teems with papers and I had no experience with it in the group of cases under discussion. Only lately have we begun the routine use of the oral administration of the sodium tetraiodophenolphthalein. Moore[3] has reported a correct diagnosis of gall-bladder pathology by cholecystography in 92.5 per cent of 55 cases in which the diagnoses were confirmed by operation.

The exact function of the gall bladder is still hidden from us. Is it a vestigial organ, a diverticulum, of the primitive biliary tract? Does it serve for purposes of storage? Since McMaster has shown that the gall bladder of the dog can concentrate bile to about one-tenth of its original bulk this explanation becomes more tenable. I can remember the time when the surgeon would point out the black viscid bile as pathologic, when he found no gall stones at operation. Lyon uses this fact to demonstrate his "B" bile. We never see this concentrated bile in the gall bladder with markedly diseased walls. This concentration may be termed a sort of physiologic stasis during periods of rest in digestion. Pathology may occur when the cholesterol of the bile crystallizes into the clear single gall stone occasionally encountered. But suppose that pathologic stasis occurs, from various causes, bacterial action may produce a catarrhal cholecystitis or a mural cholecystitis, and with precipitation of the bile pigment the multiple calcium-pigment stones appear.

In 1905 I suggested that an occasional cause of gall-bladder infection might be the passage of microörganisms from the liver to the gall bladder through the superficial collecting lymphatics. Graham believes this is the frequent route and regards hepatitis as concomitant with cholecystitis. Heyd has worked on similar lines. So we are gradually coming to regard gall-bladder infections as part of infection of the whole biliary system. The clinical studies from Lyon's laboratory point to the fact that he regards the gall bladder as of lesser importance, except in so far as surgery must remove it, in his method for artificial drainage of "poisoned bile."

Thus the liver is brought into prominence and a great deal of effort has been made to devise a method whereby liver function can be measured. So far these efforts have been balked by the apparent fact, as shown by Mann, that a considerable amount of the liver can be removed and the animal live and its liver function. The test devised by Rosenthal is that most commonly used. Further studies of the liver function lead us to suspect that the bile pigments are not formed in the true liver system. McNee follows Aschoff in believing that cells of the reticulo-endothelial system elaborate the bile pigment. Then cells occur in the liver, spleen, bloodvessels and in other parts of the body, the larger portion being found in the walls of the blood sinuses of the liver and known as Kupffer cells. The polygonal cells of the liver probably play no part in this synthesis. The bilirubin may simply pass through them, to be excreted in the bile, or it may be chemically altered during the secretory process.

This work has led to the development of the van den Bergh, Fouchet, icterus index, and other tests which are believed to determine whether a jaundice is obstructive or hemolytic in origin. Dr. I. S. Ravdin, Dr. E. G. Ravdin, and myself[4] have described our experience with the van den Bergh test, but the work was only begun near the end of the series of operations here reported. We now find the test of extreme value, not as a test of liver function, but as a test of the working of the extrahepatic passages.

The taking of a minute case history is invaluable in the study of a supposed gall-bladder infection, or a case of gall stones, but it most certainly must be associated with accurate modern laboratory tests if we hope to make a high percentage of accurate predictions as to the pathology present and the possibility of successful surgical treatment. The discussion in this paper is based on the results of 128 operations on 126 patients. There were 8 deaths, a mortality of 6.3 per cent. The cases are consecutive and comprise all of the operations done by myself and my assistants except those operations on the gall bladder performed in the course of the surgical treatment of acute pancreatitis, malignant disease of the pancreas, splenomegaly and 1 case of reconstruction of the common duct. For purposes of analysis the series is divided into:

| | Cases. | Deaths. |
|---|---|---|
| 1. Acute suppurative cholecystitis | 19 | 1 |
| 2. Acute cholecystitis with common duct obstruction | 5 | 2 |
| 3. Chronic cholecystitis | 78 | 0 |
| 4. Chronic common duct obstruction | 26 | 5 |

This grouping is found convenient because the principal problems in treatment concern the management of the acute empyema, or gangrene of the gall bladder, where the question of primary cholecystostomy or cholecystectomy must be settled; the association of a common duct stone with acute suppuration of the gall bladder and possibly of the main ducts; and the management of the ordinary common duct stone, especially with marked jaundice, hepatitis and pancreatitis. The ordinary chronic cholecystitis, with or without stones, is a comparatively simple problem.

1. Acute Suppurative Cholecystitis. This group (19 cases) was characterized by clinical evidences of acute inflammation, such as tenderness, rigidity, fever and leukocytosis, and the pathologic appearance of acute suppuration. Sometimes the gall bladder was moderately diseased, but more often it was greatly swollen, intensely congested and with walls often nearly a centimeter in thickness. The evidence of edema was conspicuous. The liver in the vicinity of the gall bladder usually showed the appearance of congestion. In 15 cases the gall bladder contained multiple stones, in 3 a single stone and in 1 there were no stones. Cholecystostomy was performed five times with no deaths; 2 of the patients required a cholecystectomy later. Cholecystectomy was done on 14 patients with 1 death. The notes on this patient were as follows:

Mrs. McG. (No. 454), aged fifty-four years, very stout. Four attacks of biliary colic, starting one year ago. Had typhoid fever at age of fourteen; acute appendicitis with operation eleven years previously. Admitted, University Hospital, November 20, 1922, suffering from pain, fever, a leukocytosis of 25,400 and a distended gall bladder. She was slightly jaundiced. The lungs were clear and the heart sounds regular and of good quality. The diagnosis of epyema of the gall bladder was made.

Operation performed the following day under gas-ether anesthesia and lasted forty minutes. Transverse incision. A large, acutely inflamed gall bladder containing pus and many stones was found. Cholecystectomy was done and three drains introduced. There were no anesthetic complications. I saw her at about 10 P.M., and was rather pleased with her condition, although she was very restless and a little irritated because we could not get her off to sleep. Her temperature was about 102° and the pulse 128. She was given a small dose, 1–200 gr., of scopalamine because I did not want her given any more morphine. At about the same time she voided 5 ounces of urine and was not at any time uremic. At 12 o'clock the temperature was 102° and the pulse 120; at 2:30 P.M. the temperature and pulse were practically unchanged. At 3 A.M. the nurse noted that the patient's circulation suddenly had failed; a few minutes later she was given intravenous saline solution and other stimulation, but failed to respond and died at 4 o'clock, eighteen hours after operation.

As no autopsy was allowed, we can merely speculate upon the cause of death. Acute dilatation of a fatty heart weakened by disease, sepsis and the shock of operation, is the most probable cause. Three points for discussion are suggested. Should immediate operation be performed in these cases, or is it justifiable to wait for some days in the hope that eliminative measures and the use of digitalis will improve the condition of the patient? I think that no hard-and-fast rule can be followed. While there is not the same urgency as in acute appendicitis, nothing particular is gained by a long delay. I usually wait for twenty-four to forty-eight hours only. The fact that there was only 1 death in 19 cases (5.3 per cent) shows that we got along fairly well. Perhaps it would have been better to have employed local anesthesia but I am partial to cholecystectomy and find local anesthesia most difficult in stout people when removal of the gall bladder is contemplated. Nitrous oxide or ethylene rarely suffices and some ether is usually necessary. On the other hand, cholecystostomy can be done readily under local anesthesia and perhaps should be considered the operation of choice in this group, particularly if the surgeon has not had much experience. A large percentage will require a second operation later, but the ultimate mortality is the important thing to hold in mind. Cholecystectomy is easy to do, except in those cases which have perforated and are surrounded by a local abscess. Troublesome oozing from the inflamed liver bed is the principal complication and as packing is fraught with later danger I think that on the whole cholecystostomy is safer.

2. Acute Cholecystitis with Common Duct Obstruction. This group, fortunately small in number, gave me a mortality of 40 per cent in 5 cases. In 2 cases the gall bladder contained multiple stones, in 1 a single stone and in 2 there were no stones. In all 5 a cholecystectomy was performed. In the 3 patients who recovered, the obstruction was caused by stone in 2 cases and pancreatitis in the other. In one the common duct and the gall bladder contained "white bile." One patient was reoperated on two months later for fistula, which was then closed.

One of the fatalities was a pure error in technic. The patient had had a cholecystostomy nine years previously and was admitted acutely ill with empyema of the gall bladder and jaundice. Adhesions were extremely dense and I so cut and injured the colon that a resection was necessary. She died two days later from peritonitis.

The other death occurred from cholangitis and hepatic depression. The notes are as follows:

Mrs. M. F. (No. 4945), aged sixty-four years. Very aged; indigestion for five years. Twenty years ago had single attack of pain associated with jaundice; always sallow; three days before admission had acute attack. Admitted with symptoms of acute empyema of the gall bladder. Leukocytosis of 20,000. Plasma $CO_2$, 48 volumes per cent. Patient was treated for a period of four days with continuous hypodermoclysis, digitalis, etc.

Operation January 31, 1925, local anesthesia. Gall bladder was found filled with stones and was removed. No exploration was done of the common duct, but a tube was pushed through the cystic duct and established drainage. The liver was extensively involved, with biliary cirrhosis. The patient became drowsy and the blood-urea showed 72 mg. per 100 cc. On February 6, it was thought that she was on the road to recovery, but two days later the temperature and pulse began to rise. In spite of all treatment death occurred fifteen days after operation. No autopsy was obtained.

I will not comment at length upon this group, the gall bladder problem is similar to that in the first group and the common duct problem to that in the fourth group. Here we have both combined and the patient must react against the sepsis and the obstruction to the bileflow. Note that in the second fatality the common duct drainage was attained by the simplest method possible, namely, the utilization of the stump of the cystic duct. Cholecystostomy alone is useless, as a rule, because several days will elapse before bile will flow through the cystic duct, obstructed as it is by the inflammatory swelling. The common duct must be tapped, although the stone should not be sought by "spooning." It can be removed if immediately accessible. Even with the best technic the outlook in these cases is always serious.

3. Chronic Cholecystitis. This constitutes the largest group and includes 23 cases of simple cholecystitis and 55 cases of calculous cholecystitis (9 single stones and 46 multiple stones). Cholecystectomy was performed 73 times and cholecystostomy 5 times. There were no deaths in either series. In 36 cases the cholecystectomy was the only operation performed; additional procedures were done on 38 patients, removal of the appendix (30 times), gastrojejunostomy (5 times), miscellaneous gynecological procedures (5 times). Rammstedt pyloroplasty, appendix stump, adhesions and excision tuberculous mesenteric glands, 1 each. Twice a cholecystostomy was followed by cholecystectomy.

Cholecystectomy for noncalculous disease was considered indicated when the gall bladder was evidently diseased by reason of thickening, pericholecystic adhesions or the aspiration of "bile-mud." In 1 case a cholecystostomy was done. The patient was jaundiced and the preoperative diagnosis was carcinoma of the pancreas. Nothing except extensive adhesions was found as a cause of the jaundice. Cholecystostomy was thought to be the safest treatment and two and a half years later the patient reports that he is perfectly well. The fistula closed in one month.

Cholecystectomy has been the operation of choice in calculous disease of the gall bladder and I cannot be convinced that simple drainage offers permanent cure in any degree comparable to removal. The literature is filled with evidence that bears this out and need not be quoted here. Naturally there may be cases where the presence of pancreatitis may seem to justify bile drainage, but if the gall bladder is in good condition internal drainage (cholecyst-gastrostomy, etc.) is better than external and if the gall bladder is extensively diseased it is probable that the cystic duct is occluded. The fact that there were no deaths after cholecystectomy in this group shows that the operation is safe enough. The end-results will be considered later. Two patients had had a previous cholecystostomy elsewhere and had a recurrence of gall stones.

Five patients had coincident gall-bladder disease and duodenal ulcer. In 4 the gall bladder contained multiple stones, in 1 there were no stones, but the gall bladder was thickened and adherent and considered primarily involved. In all a posterior gastrojejunostomy and a cholecystectomy was performed. In 3 the appendix was also removed. In 1 patient I performed a Rammstedt operation because the pylorus seemed small and stenotic. As noted the appendix was removed many times, sometimes through the upper transverse incision almost always used, and sometimes through a separate McBurney incision. The association of appendicitis and gall-bladder disease has been much discussed, and without proper investigation I am inclined to think that in the absence of an acute attack the etiologic factor of the appendix is usually exaggerated. The percentage of crooked, adherent appendices will be found just as great when operating for fibroids of the uterus as for gall stones.

4. Chronic Cholecystitis and Common Duct Obstruction. This group comprised 26 cases with 5 deaths (19.2 per cent). Thir-

teen patients had multiple stones in the gall bladder and stones in the common duct. Cholecystectomy was done, the stones removed from the common duct and the duct drained with a T-tube; 3 of these died. In 3 cases the gall bladder was removed for multiple stones and the common duct found to contain "white bile." The duct was drained, the obstructing stone not being seen nor felt. Pancreatitis was present and might have been the cause of the obstruction; 2 of these patients died but the third, a woman aged seventy-six years, deeply jaundiced, recovered and is well seven months after the operation. Four patients had stones in the gall bladder but none in the duct. They recovered after cholecystectomy and duct drainage. Three patients had duct stones but no gall-bladder stones and 2 had no stones; all recovered after cholecystectomy and duct drainage. One patient had a cholecystectomy three years previously and was found to have duct stones. She recovered.

It is evident that, from the standpoint of mortality, this group is the most important one, and while we may be caustic in our criticism of patient or physician for delay yet the fact remains that the surgeon must rescue the patient. There is not space to discuss many of the points involved. The patient must be prepared by the method best brought out by Walters, of the Mayo Clinic. Haste is rarely indicated and three or four days of preoperative preparation are absolutely necessary. Water, glucose, calcium chloride and perhaps digitalis are the main things. From some recent experience I am inclined to think that a well-executed nonsurgical drainage carried on for a few days is helpful. Sweet thinks that ether is a liver poison only second to chloroform, hence ethylene or nitrous oxide reinforced by novocaine locally is the anesthetic of choice. Sometimes local anesthesia alone suffices, but I have not been able to manage choledochostomy and cholecystectomy by local anesthetics.

Cholecystostomy is easily done under local anesthesia, and in the very ill patient, with a high van den Bergh test (10 to 12 units, for example) without tight jaundice, with some fever, some mental depression, or with a high degree of blood-sugar, close attention should be paid to the gall bladder to see if the cystic duct is patulous or not. If so, a primary cholecystostomy is the operation of choice. Those who are very obese, are severely jaundiced, have a high blood-pressure and interstitial nephritis, are also grave risks. If the gall bladder is not capable of draining bile, the common duct must be

opened and the liver drained; but, except in those only moderately ill, "spooning" of the liver ducts and retroduodenal pressure or trauma must absolutely be avoided. It is true that many patients, quite sick, recover after a complete operation, but the group mortality is too high and the two-stage procedure must be extended if we want hope of having less deaths. The following is an example of the sequence of events in a fatal case.

Mrs. A. P. (No. 3346), aged fifty-one years, emaciated. Symptoms began acutely seven months previously, followed by numerous attacks. Admitted intensely jaundiced and suffering pain. Says she has lost 120 pounds in weight in the last six months. Blood-pressure was 140 systolic and 90 diastolic. She was treated in the medical wards for a week and then transferred for operation.

Operation April 22, 1924. Novocaine local and gas anesthesia. Duration one hour. The gall bladder contained two stones impacted in the cystic duct and was removed. The common duct was opened and contained a lot of soft pigment. The common duct was evidently compressed by the stones in the cystic duct. When the T-tube was introduced, bile began to flow freely. The liver looked markedly cirrhotic. Following operation the patient steadily declined, although draining large quantities of bile. Blood transfusion was done, but the patient soon developed the low blood-pressure and the weak though not rapid pulse that we have associated with pancreatic asthenia. Death occurred ten days after operation. Autopsy showed no obstruction of common duct and the pancreas appeared grossly normal.

The other deaths in this group occurred, 9, 12, 16 and 17 days after operation, giving an average of 12.8 days for the 5 patients. Apparently death occurred from what has been termed cholemia, or, as Heyd expresses it, from liver exhaustion. None of the patients died early from vasomotor depression, but I have seen this type of death several times. I can remember 1 death in the third group described by Heyd in which coma occurs almost immediately after operation and early death results. He says it has occurred after rather simple types of operation on the biliary apparatus, and, with Killian, he has found such patients show a very high carbon dioxide combining power representing as much as 80 to 100 volumes per cent.

Jaundice is a symptom and indicative of obstruction, but takes on supreme importance because nearly all of the fatalities occur in the group in which it is manifest. In my series 7 of the 8 patients who died were jaundiced. In the group operated on in the University Hospital, 31 (40 per cent) stated that jaundice has been present during one or more of the attacks. In 11 the gall bladder

only contained stones and 1 case was noncalculous. In 3 patients stones were present in the common duct, but there was no jaundice. This finding is important because it represents 6.5 per cent of the group and shows the supreme importance of palpating the common duct in all cases. There is another feature of importance, the failure to detect stones even by palpation. Kehr[5] found that 46 per cent of 36 cases in which palpation of the common duct was negative had calculi in either the hepatic ducts or retroduodenal part of the common duct, and Eisendrath,[6] in a series of 34 cases in which palpation was negative, found after choledochotomy that he was wrong in 32.3 per cent of times. Perhaps the old rule of Kehr is a good one—the common duct should be opened when the duct is dilated and thick-walled, when there is pancreatitis, and when the gall bladder or cystic duct contain numerous small stones. In the 11 cases of this series in which a history of jaundice was elicited, the trouble apparently confined to the gall bladder and only a cholecystectomy done, every patient has been traced and with one exception is perfectly well; he complains of some "gas" after meals. This series should be watched over a period of years.

Recurrence. Ten patients in this series had multiple operations on the biliary tract; 4 had had a previous cholecystostomy done elsewhere and required a cholecystectomy; in 2 cases we did a cholecystostomy and later removed the gall bladder; 1 patient was reoperated upon by Dr. Godfrey for stricture of the common duct due to adhesions, 1 for a common duct fistula and 1 for a cystic duct leak with "bile cyst," 1 patient had had a cholecystectomy done by me in another hospital three years previously and returned with a duct stone. None of the patients in this series has so far suffered from recurrent symptoms due to duct stone.

End-results. An effort was made to trace the end-results of these patients and either personally or by letter the condition of the patient ascertained from six months to two and a half years after operation.

| | Cases traced. | Well. | Improved. | Unimproved. |
|---|---|---|---|---|
| Acute cholecystitis: | | | | |
| Cholecystectomy | 12 | 11 | 1 | 0 |
| Cholecystostomy | 4 | 3 | 1 | 0 |
| Acute cholecystitis and duct stone | 2 | 2 | 0 | 0 |
| Chronic cholecystitis: | | | | |
| Without stone | 20 | 11 | 7 | 2 |
| With stone | 38 | 30 | 5 | 3 |
| Common duct stone | 15 | 12 | 3 | 0 |
| Total | 91 | 69 | 17 | 5 |

The improved group (18.7 per cent) are nearly well. Some still suffer from "gas" and some complain of adhesion pains. One patient had severe colic with jaundice and was reoperated on elsewhere but only a constricted common duct was found. Eight months later he reports that he is well. Three patients died after leaving the hospital, one from chronic pancreatitis, one from intestinal obstruction in the lower abdomen, and one after an operation for adhesions. This patient had had a cholecystostomy elsewhere, came to me for persistent trouble and I removed the gall bladder. Later, her symptoms returned and she again returned but died after the third operation. One of the unimproved cases had had a previous cholecystostomy and there were many adhesions. In 3 of the improved group certain abdominal complications may be responsible for further trouble. This "follow-up" study dates to November 1, 1925, and a more detailed report will be made in a second paper after at least one year has elapsed since the last operation of the series. It would seem as though a final good result in at least 90 per cent of the cases speaks well for surgical treatment.

In considering end-results we must remember that after diet, medicine and duodenal drainage, remissions frequently occur and irreparable liver damage done before operation is advised. The patient may recover but the infection in the gall bladder persists and acts as a focus of infection for other organs. McMaster[7] experimentally has shown that the output and concentration of cholesterol in the bile are subject to profound modification by dietary influence. When a ration rich in cholesterol is given, the amount of the substance in the bile greatly increases. This work has led us to give our patients a diet sheet similar to the one advised by Moynihan.[8] The relation of diet to postoperative symptoms is also well discussed by Wilenski,[9] who emphasizes the importance of a diet free from fats and lipoid bodies.

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## DISCUSSION

Dr. J. E. Sweet: It seems a particularly embarrassing moment to call upon me to discuss a subject concerning which there are only three people in the world who have definite knowledge, and of these three one is about to present a paper on the subject and the other two are about to discuss his paper. Nevertheless, in the review of these interesting cases presented by Dr. Müller, a number of things occur to my mind.

The first question is, Should the same operative procedure be applied to all cases of gall-bladder disease? As we look back upon the history of gall-bladder operations we find a time when cholecystostomy was considered a certain cure. Then cholecystectomy was suggested and cholecystostomy passed out of style, probably because the removal of the infected gall-bladder and the opening of the infected lymphatics more closely approaches the site of the difficulty than does the simple drainage of the gall-bladder. We must remember that the infection is not catarrh of the mucosa, but is a lymphangitis of the wall of the gall-bladder. But where is the infection in the long-standing chronic case with involvement of the entire duct system? Here, again, the infection is in the lymphatic system, and an attack upon the gall-bladder alone will not necessarily reach the entire infected area. The most obvious and physiologic answer to the question is earlier diagnosis of the disease, earlier operation; but that does not help the surgeon to whom such a long-standing chronic case has come. It seems to me it might be logical to think of the possibility of draining the lymphatics around the head of the pancreas. I admit that the suggestion would not be a safe one in all hands, because a free scarification of this region might result in damage to some of the important structures lying in this area. Nevertheless, the problem is one of infection and of where drainage should be placed.

Another interesting problem is the peculiar reaction of some of these cases to operative procedures. How much of the curious result you see recorded in some of the cases presented by Dr. Müller is due to the disturbance of the function of the gall-bladder? This problem, the function of the gall-bladder, remains in the hands of the physiologic chemists, who must tell us the function of cholesterol in the body.

# CYTOPLASMIC RÔLE OF THE LIVER *

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I DEEPLY appreciate the opportunity your invitation gives me for presenting a phase of our attempt—futile though it may be—to throw light on the nature of living processes by means of a biophysical approach.

Our premise is that the living and the nonliving are chemically identical, the living differing from the nonliving not in substance but in the utilization of nonliving material for the construction of mechanical devices that have the power of transforming energy and of reproducing themselves.

In accordance with our theory, these processes which distinguish the living from the nonliving are due to electrical forces within the protoplasm, which endow the protoplasm with the essential qualities of irritation, assimilation and reproduction. It is due to these electrical processes that groups of the protoplasmic energy units become associated in cells. Within the cells identical electrical forces produce the mitotic processes by means of which are formed the paired identical parts, each of which forms a new cell. And even before the protoplasm is formed, electric forces arrange the atoms and molecules as building stones, each in its own place, to form the essential structures of the protoplasm.

Moreover, not only do electric forces construct the component structures of the cell, but they arrange the atoms and molecules of the structures outside the cell which play their part also in rendering effective the electric charges created within the cell itself.

In accordance with the bipolar theory, we believe that the potential within the cells is created by variations in oxidation on the two sides of the condenser plates—films—which separate the nucleus of

* Read November 4, 1925.

the cell from the cytoplasm and the cytoplasm from the surrounding medium. Thus, in each of the trillions of cells of the body there is created an electric strain, the vibratory discharges of which serve as the catalyst which produces oxidation, oxidation in turn renewing the electric charges on these countless interfaces within the cells.

Thus the specific characteristic which differentiates the living animal organism from the nonliving materials of which it is composed would appear to be the vibratory frequency and force of these electric discharges rather than its static structure. An animal is an energy phenomenon rather than a form phenomenon, the energy being electric and vibratory.

On the basis of this assumption, it is necessary to identify the original source of the vibratory forces which transmitted this characteristic to the atoms and molecules of the colloids within which the first living organism arose. This we may assume to have been the vibrant energy of light which obviously is the ultimate source of life. We thus assume that life may be defined as the expression of the specific energies emitted by atoms and molecules, which energies in turn were given them by light. In accordance with this conception the composition of the living organism must be constantly changing; and electric energy governs the composition of the structure of the organism and the composition and arrangement of the structure in turn makes possible the transformation of energy. That is, the energy and structure of the organism is constantly changing and yet apparently the structure and the energy remain constantly unchanged.

An analogy to this cycle of static and kinetic changes within the organism is offered by the rainbow, which appears to be static and stationary although rays of light are swiftly passing through the swiftly falling drops of water. The rainbow seems to be static because the effect of each wave of light on each drop of water is the same as that of its predecessor. In other words, the rainbow is the result of an infinite series of equal variations in electric strain among an infinite number of atoms and molecules, the arrangement of which is stationary and characteristic although the atoms and molecules which constitute that arrangement are constantly changing.

We may imagine that by the vibratory electric forces of light a positive charge was transmitted to infinitely small particles of matter of ultramicroscopic size, thus producing a difference of potential between these particles and the negative electrolytic solutions in the

sea or in the mud which surrounded them. When this difference of potential reached a certain point we may conceive that a discharge took place with an immediate rebuilding of the differences of potential, this process continuing until these small particles of matter built up a permanent mechanism for the maintenance and interchange of electric forces—thus creating the first mass of protoplasm. This small mass of protoplasm by its greater power of oxidation would have been positive as compared with the negative electrolytic solutions by which it was surrounded, and therefore by a like process of discharge and immediate rebuilding of potential would have finally permanently acquired an electronegative portion which became the cytoplasm of the first cell.

By the continuance of these alternative processes created by an alternation of electric strains and discharges, we may suppose the primary cell or cells grew and became increasingly complex until by some fortuitous circumstance some cell divided but the daughter cells did not separate. Groups of cells then specialized, each along essential lines for the most efficient acquisition of each of the factors essential for its specific energy—sunlight and oxygen. Thus through constant changes, as the result of fortuitous circumstances, form after form was evolved, each becoming more complex as the range of responses widened. For the unified responses of the more complex mechanisms the bipolar arrangement continues to exist, positive electric forces becoming centralized in certain tissues and negative forces in other tissues.

That is, if this conception be correct, there must exist in the organism not only a tissue or part of highest positivity but also a tissue or part of lowest negativity. That is, one part of the electric circuit must be "grounded." According to this conception, the organism would contain an aggregate of cells which contains more earthy colloids, more neutral or alkaline compounds than any other organ or tissue. And in order that this high degree of neutrality or alkalinity may be maintained such an aggregate of cells would have a large intake of neutral salts, and the cells would be suspended in an abundant medium of electrolytic solutions. The rate of oxidation of the cells would be low, since oxidation is the common cause of acidity, which must be avoided by this electrically negative tissue; hence this aggregate of cells must have an abundant venous and a meager arterial supply. In order to make doubly secure the preponderance of alkalies, this tissue would be provided

with a special circulation. If such a tissue or organ were removed it would as totally incapacitate the multicellular animal as does the removal of the cytoplasm from the nucleus of an unicellular organism or as does the removal of the negative pole, or of the ground of an electric battery. Such an organ would play an especially dominant rôle during the embryonic life and development and the growth of the animal and this would be manifested in a dominant growth of the organ itself. It would collaborate with its associated positive pole or organ of highest positivity in every general function of the organism as a whole, and when the slow processes of the wear and tear of life or the more rapid processes of disease bring to the organism first exhaustion and finally equilibrium or death, the pathologist would find that the cells of this negative tissue, like the cells of the opposite positive organ, would uniformily show swelling, rupture of cell membranes and loss of nuclei. If such an organ were removed its loss would be irreparable. There would be no possible substitution. Its removal would inevitably be followed by a steady, continuous lowering of temperature, progressively diminishing energy and death.

Like the cytoplasm of the amœba, such an organ would show an affinity for acid metabolites; and unlike its opposite pole, by virtue of its negativity, it could store food solutions without endangering its function. It would attract all sorts of battery waste, thus keeping the opposite pole clear; and when deprived of a steady supply of neutral or alkaline material it would lose its degree of negativity, hence its power of keeping the circuit clear, and acidosis would develop. Such an organ would show a pronounced affinity for acids in excess, but when the acids are produced as rapidly as in excessive exertion, excessive emotion, excessive fever, or when the elimination of the excessive acids is interfered with, as in pneumonia, in asthma, in failing circulation, in inhalation anesthesia, this negative or clearance pole or organ would become so disabled that it would be unable to neutralize all the acids, and the cells of the kidneys—intended as a filter—would become seriously damaged. Thus under such circumstances we would expect to find that not only the negative organ but also the kidney and the heart would be affected. Such an organ, therefore, would be one of the hardest-worked organs in the body; it would show changes in structure and function in every stress in life; it would work and sleep, live and die in consonance with its opposite member. The cytoplasm of the

unicellular organism receives for the nucleus and for itself all the food required for both: it discharges the waste products of both. It serves as the opposite pole to the positive nucleus. For man and animals the liver receives the food for the body: the liver is the principal organ of elimination. It would appear, then, that the liver plays the rôle of cytoplasm, that it is the negative pole of the organism, playing always with what we assume to be the positive pole—the brain.

That the liver primarily represents certain essential functions of the cytoplasm is suggested by many facts, among which the following are of especial significance:

1. The cytoplasm of the unicellular organism receives and stores food; the liver receives and stores food (glycogen).

2. The cytoplasm of the single cell picks up and has an affinity for the acid by-products produced in the nucleus and in the cytoplasm itself; in the higher animals the liver plays a similar rôle.

3. The nerve cells, like the nuclei of unicellular organisms, possess no neutral fat, no glucose, no acid-neutralizing material; these are stored in the liver for the benefit of the brain as well as for itself and for other organs and tissues.

4. In the amœba neither the cytoplasm nor the nucleus can function without the other; in the higher animal the brain cannot function without the liver; the organism cannot function without the brain. The brain and the liver work simultaneously; the brain and the liver are restored simultaneously.

5. The early evolutional appearance of the liver is significant. Although the function of the so-called hepatic cells of the polyps has been disputed, nevertheless the gradual concentration and development of these cells from the polps through the echinoderms, annelids, insects, etc., to the fishes, reptiles, birds and mammals, make it appear that the peculiar functions of the cytoplasm which we have described above began to be assigned to specifically differentiated cells (liver) at a very early period in evolution.

6. In the embryo the anlage of the liver appears in the very earliest stages of development, *being practically coincident with the appearance of the anlagen of the central nervous system*. The embryonic development of the liver is exceedingly rapid, the organ almost filling the abdominal cavity in the third month, when its weight is approximately 10.5 per cent of the entire body weight;

throughout life its weight is usually about 2 per cent of the entire body weight. As Keibel and others have stated, the precocious appearance of the anlagen of certain organs *is undoubtedly associated with the necessity for their early development*, the anlagen mutually influencing each other in the development of the organism as a whole.

In addition to these facts which would appear to suggest the cytoplasmic origin and function of the liver, many facts may be cited which indicate not only the interdependence of the brain and the liver but also their antithetic rôles in the organism. These facts indicate, also, that this interdependence is due to some relationship which is not explained by any current theory. How, for example, can we account for the progressive changes in the brain and the inevitable death which follow the excision of the liver; or for the alternation in the functioning of the brain when the liver is damaged? These changes are not due to a want of glycogen, for the administration of glycogen does not prevent death. It does not seem that death after hepatectomy can be due alone to the loss of the power of the liver to split up acid by-products for the following reasons: (1) Life is not prolonged by the administration of large doses of morphine for the purpose of minimizing metabolism and in consequence diminishing the amount of acid by-products; (2) the repeated transfusion of blood does not prolong life; (3) the administration of acid-neutralizing alkalies is of no avail. It would seem that the dramatic fall in body temperature might be an important factor in the inevitable death which follows excision of the liver, but the maintenance of the normal temperature by artificial means does not prevent death. No therapeutic measure has been found of avail in acute yellow atrophy of the liver or after the excision of the liver.

In addition to the fact that death is the inevitable result of excision of the liver, there are certain other outstanding facts which cannot be interpreted by any conception of the method of operation of the organism which has thus far been proposed. Among these the following are of especial significance:

1. When the adrenals are removed the liver cells with the brain cells undergo a physical disintegration. Neither the brain nor the liver can survive without the adrenals.

2. After decapitation, if the adrenals remain intact, the liver cells do not break down.

3. The injection of adrenalin increases the stainability of the brain cells and the liver cells.

4. The liver and the brain, and to a lesser degree the adrenals, are affected simultaneously by any cause of exhaustion. These organs work and are exhausted simultaneously; they are restored simultaneously.

5. Want of oxygen causes loss of brain function and death. Want of liver function causes loss of brain function and death. These facts suggest that nerve cells require for their action the presence of oxygen, of adrenal function and of some rôle played by the liver.

6. In every experimental test the liver has been found to be exceedingly sensitive to change, even more so than the brain. This was shown in resuscitation experiments; in perfusion experiments; by observations of its unequalled rapidity of autolysis; and by measurements of its electric conductivity.

7. In his studies Renauld-Capart noted that "the first fact established was that the abdominal blood is essential to the function of the brain centers. This being demonstrated, we directed our research to discover which of the abdominal organs could so affect the blood as to influence the cerebral activity. We have from the very first established that the blood which passes through the liver has the property of reëstablishing cerebral functions; following this, that the liver alone, of all the abdominal organs, has that property."

8. The chemical constitution of the liver is in harmony with the conception that it is the negative pole of a bipolar organism. The liver is rich in mineral substances—potassium, sodium, phosphoric acid, chlorin, iron and alkaline earths. The tendency of the liver cells to accumulate mineral substances, especially metals, has been emphasized by Roger. On the other hand, the metallic content of the brain is exceedingly minute as compared with the liver.

Finally, and of prime importance, are the biophysical findings that the application of any stimulus causes opposite changes in the conductivity of the brain and of the liver. Thus, in the stage of stimulation by any agent, the conductivity of the *brain is increased;* the conductivity of the *liver is decreased*. In the stage of exhaustion, the conductivity of the *brain is decreased;* the conductivity of the *liver is increased*. In like manner, the temperature changes in the brain and in the liver tend in opposite directions.

This evidence certainly shows the interdependence of the brain and the liver and strongly supports the assumption that while the

brain cells are purely oxidizing mechanisms, the liver, which is the only organ in the body supplied with venous blood, is in effect an earthy solution, certainly negative, and therefore a most suitable medium for "grounding" electric currents.

From these premises we conclude that the liver is an organ which performs a major and essential function in the organism. These premises, moreover, explain not only why the liver is impaired by any condition which impairs the organism as a whole, but also why the organism as a whole is affected by anything which impairs the liver function. In the light of these premises, also, we are directed to certain measures which have a conserving and restoring effect upon the organism as a result of their effect upon the liver. The essential function of the liver in the assumed bipolar mechanism is such that if it is functionally impaired, to the extent of that impairment will the ability of a patient to undergo an operation upon any part of the body be diminished and the surgical risk accordingly increased, especially if of itself it lessens further the activity of the liver. In planning the management of surgical operations, therefore, it becomes of prime importance to find how the function of the liver can best be protected. It is obvious that water and alkalies are of primary importance if the essential alkalinity of the liver is to be maintained. Circulation of blood must be maintained. As we have indicated above, the function of the liver and the function of the kidneys have an important interrelation and in order that the optimum function of each may be maintained an optimum circulation of blood is essential. In addition to water and alkalies and an adequate circulation, however, there is another essential factor the importance of which has not been comprehended. It is a biophysical law that a change of 1° in temperature changes the chemical activity of either a physical or biological system 10 per cent. Therefore, when the temperature of the liver is reduced 1° its chemical activity is reduced 10 per cent. Therefore, if in any patient as the result of the exhaustion incident to his disease, as in cancer of the stomach, for example, the chemical activity of the liver has already been reduced to 10 per cent of its normal capacity, then, if when the abdomen is opened the temperature of the liver is reduced but 1°, death will follow inevitably.

In an attempt to discover to what extent the temperature of the liver may fall in abdominal operations, a research was undertaken in the Biophysics Laboratory of the Cleveland Clinic Foundation, in

which it was found that when the abdomen was opened, even if the liver itself was not directly exposed, the temperature of the liver fell from $1\frac{1}{2}°$ to $3°$ or more, and the impairment of the organism as a whole as a result of this lowered liver temperature was indicated by the fact that the temperature of the brain also fell from $1°$ to $3°$ This progressive fall in the temperature of the brain in these cases was identical with that which followed the removal of the liver. Moreover, in animals under ether anesthesia a similar lowering of the temperature of both the liver and the brain was observed. Under nitrous-oxide anesthesia, on the other hand, the temperature of the brain and of the liver was but little altered.

A lowered blood-pressure induced by hemorrhage also lowered the temperature of the brain and of the liver. The lack of ability of the organism as a whole to function in the absence of the liver function was demonstrated by the lack of response of the brain to the injection of adrenalin after the liver was removed. That is, normally the brain responded to the injection of adrenalin by an immediate increase in temperature of from $0.5°$ to $1°$, but after the removal of the liver the injection of adrenalin produced but little or no change in the temperature of the brain. In view of these findings one can well understand why the mere exposure of the abdominal viscera may cause death in a very sick patient even if no operation has been performed and no general anesthetic has been administered.

We can understand, also, why the addition of the general anesthetic and of the operative procedure to the exposure of the intestines may cause the death of the patient who may not be so desperately ill.

This fatal sequence of events was illustrated on a large scale during the World War by the effects of abdominal operations performed during the winter months in the front-line hospitals, where but few soldiers survived an abdominal operation, especially when the operation required a wide exposure of the abdominal viscera. It apparently made no difference how quickly or how skilfully the operation was performed.

Another remarkable fact established by our laboratory research was that the introduction or application of heat within the abdomen, which in most of our experiments was accomplished by the introduction of hot water into the stomach, produced not only an immediate rise in the temperature of the liver but also a rise in the temperature

of the brain; and of special significance was the observation that the rise in the temperature of the brain occurred one minute or even more before the increase in the temperature of the liver was noted.

It would appear, therefore, that the application of heat to the liver should counteract the effect of the exposure of the viscera in an abdominal operation upon any patient, and in particular in operations on the liver or on the bile ducts.

Attempts have been made to meet this requirement by hot-water pads, hot tapes, the use of the hot-water mattress, and a superheated operating room, but none of these methods has satisfactorily met this crucial need.

Recently it occurred to me that the application of diathermy would be an ideal method for holding the temperature of the liver at or about the normal level. The principle of diathermy is that passage through the tissues of a current from a specially devised apparatus heats the tissues. Therefore, if one pole of the diathermy apparatus were placed upon the lower chest on one side and the other brought opposite the dome of the liver, then the current would pass through the upper abdominal organs, including the liver; and since this current would be continuously applied during the operation the temperature of the liver and of the abdominal viscera in the path of the electric current would be maintained at or above the normal regardless of the exposure of the intestines. It must be borne in mind that, on account of the enormous spread of the capillaries, veins and arteries very near the surface of the viscera, the blood in the whole splanchnic area almost immediately assumes the temperature of the air to which it is exposed. It is almost as if the blood in one part of the circulation were spread out in a thin layer on a great table and were then collected and again placed in circulation. By the passing of the diathermy current through the liver and the neighboring viscera this thin layer of blood is, as it were, made to pass over a hot table, so that warm instead of cool blood passes into the rest of the circulation.

The electrodes can be put in place and the diathermy current established before the abdominal incision is made, and neither the surgeon nor the patient need be aware that such a current is passing, as the use of rubber gloves completely insulates the hand of the surgeon.

We have found by actual observation that by this means the

temperature of the dome of the liver can be maintained above normal throughout an operation in which the abdominal viscera are widely exposed.

The higher incidence of pneumonia after abdominal operations than after operations of an equal magnitude on other portions of the body is well recognized. In view of this fact, and in view of the facts which we have cited, one might well question whether or not this is in part the result of the cooling of the blood in the important organs within the chest plus the general depressed function of the organism as a whole as the result of the cooling of the liver. We are, therefore, now noting whether or not the maintenance of a constant temperature in the liver and other abdominal viscera by the use of diathermy is lessening the incidence of postoperative pneumonia as well as operative depression.

In addition, we are using repeated doses of diathermy after operations upon feeble and aged patients, and after especially wide and prolonged exposure of the upper abdomen, delivering the dose through the bases of the lungs, as this is the area where postoperative pneumonia is initiated. In addition to the advantage of heat, the increased temperature must induce a more active circulation in this area and thus increase the defense against infection. As shown above, a lowered temperature of the liver, hence impairment of the whole organism, may be induced by ether anesthesia. While this effect may to some extent be counteracted by the application of heat, the best method of protection is to substitute for ether the anesthetic which our researches have shown produces very slight lowering of the liver temperature, namely, nitrous oxide; and, in especially bad-risk cases, not to allow the patient to pass beyond the stage of analgesia, relying principally upon regional anesthesia.

The dramatic transformation which we have observed in patients who have been brought to the operating room in almost a moribund condition has proved the paramount value of this new protective measure. This added link in the chain of clinical evidence, when combined with the mounting accumulation of evidence from laboratory investigations, appears to justify the assumption that man and animals are bipolar mechanisms constructed on the pattern of the single cell, and that in the multicellular organism the liver carries on the rôle of the cytoplasm of the single cell.

## DISCUSSION

Dr. John B. Deaver: The College is to be congratulated on having so brilliant a paper by so brilliant a man as Dr. Crile. Dr. Crile's ingenuity has added another obligation to the many that the surgeons of America owe him. I will not discuss the biochemical or the physiologic side of the paper, only the more practical points Dr. Crile has spoken of.

Lister was a great physiologist before becoming the great surgeon he was, as was Crile before becoming the great surgeon. There are some very practical points Crile has brought out. First, the retaining of the heat of the body in surgical operations, conserving Nature's forces: The application of artificial heat in the shape of a hot-water mattress for the operating table was suggested, as you know, by Mayo Robson years ago; later the electric mattress was used. The latter, while more practical, is also more dangerous if every care is not observed. It has always been our practice to conserve heat by having the operating room at the proper temperature, and it has been my individual practice to allow as little exposure of the abdominal viscera as possible, in the use of hot gauze pads in the abdomen, to maintain the intra-abdominal temperature.

I do many of my operations under gas-oxygen, of which Crile has been an advocate. I believe the ideal anesthetic is nitrous oxide and oxygen, with block anesthesia when practicable. Dr. Crile has brought up the question of traumatism and in his characteristic way speaks of handling the tissues "lovingly." That expresses it perfectly. It has been a privilege and a pleasure to discuss Dr. Crile's paper.

Dr. John H. Gibbon: I am sure that all who have heard Dr. Crile's paper have been impressed with the thoroughness and conscientiousness with which he has undertaken this interesting study. I am afraid that a good deal of the physics which he has given has not altogether been understood, but as usual his paper closes with practical conclusions full of suggestions and interest. Dr. Crile's excellent work on anoci-association was presented in very much the same way as the subject he discusses tonight. At first it was thought by many to be only of scientific interest, but as a matter of fact all surgeons, especially those doing thyroid surgery, profited in a very practical way from Dr. Crile's work. Every now and then there occurs a death after a gall-bladder operation that is inexplicable. They are not septic deaths; they are not due to what is ordinarily called shock, and it seemed to me that in what Dr. Crile has given us tonight may be found their explanation. In his work on anoci-association he showed us the dangers of "cold feet," and now he is demonstrating the danger of a "cold liver."

I should like to emphasize the importance of one point made by Dr. Müller. It is the necessity in all gall-bladder operations of carefully determining the condition of the common duct. The duct should not only be palpated, but seen, and if it is dilated or if the patient has had common duct symptoms the duct should be opened.

Dr. Crile (closing): I rise only to thank the gentlemen who discussed my paper and the audience for so patiently listening to what I had to say.

# SURGERY AND DIABETES*

By ARTHUR E. BILLINGS, M.D.

It has long been known that any kind of surgical operation on a diabetic patient entails more risk than a similar operation on a nondiabetic individual. Poor reaction to anesthesia, marked susceptibility to infection and gangrene, and increased liability to the development of postoperative complications such as poor wound-healing, pneumonia, acidosis and coma have made this group of patients one of the most dreaded in medicine from a surgical point of view.

This danger has maintained largely until the last decade. The development of our present-day knowledge of blood chemistry and metabolism, the establishment of scientific dietary standards by Allen and the discovery of insulin by Banting and his co-workers have done much to remove the special hazard that formerly attended operative procedure on the diabetic patient. Improved operative technic, more care in preoperative preparation, wisdom in the choice of the anesthetic and greater skill in its administration are also factors that have played some part in reducing the mortality rate.

As a group, aside from the special dangers enumerated above, diabetic patients are poor operative risks. One outstanding reason for this is the frequent association of other constitutional diseases, the most common of these being arteriosclerosis, chronic nephritis, heart disease, syphilis and tuberculosis. The association of one or more of the above-named diseases with diabetes at once becomes a factor in lowering resistance to acute infection and increasing the dangers of anesthesia and operation for any condition. Arteriosclerosis and early senility are conspicuous accompaniments of the disease.

* Read December 2, 1925.

In this connection we are using the data obtained from 325 consecutive admissions representing 291 patients suffering from diabetes at the Pennsylvania Hospital. These admissions cover the period from January 1, 1915 to November 15, 1925.

| | |
|---|---|
| Patients admitted suffering from diabetes | 291 |
| Readmissions | 34 |
| Total | 325 |
| Total deaths (approximately, 15.5 per cent) | 45 |
| Total number refusing treatment and leaving hospital against advice (19.5 per cent) | 57 |

Associated Disease

| | | |
|---|---|---|
| Arteriosclerosis | 88 cases | (30.2 per cent) |
| Chronic nephritis | 43 cases | (14.7 per cent) |
| Heart disease (endocarditis myocarditis) | 42 cases | (14.4 per cent) |
| Syphilis* | 26 cases | ( 8.9 per cent) |
| Tuberculosis | 24 cases | ( 8.2 per cent) |

Surgical Complications or Conditions Not Operated Upon

| | |
|---|---|
| Ulceration and gangrene of one or more toes | 25 cases |
| Abscesses, carbuncles and cellulitis | 11 " |
| Gall-bladder disease | 3 " |
| Toxic goiter | 5 " |
| Carcinoma: | |
| Breast | 1 " |
| Jaw | 1 " |
| Uterus | 1 " |
| Prostate | 1 " |
| Duodenal ulcer | 1 " |
| Hydrocele | 1 " |
| Undescended testicle | 1 " |
| Hernia: | |
| Bilateral inguinal | 1 " |
| Umbilical | 1 " |
| Varicose veins | 2 " |
| Fractures: | |
| Humerus | 3 " |
| Ribs | 1 " |

Operation was not done on many of these cases because the indications did not seem sufficiently strong to justify it or on account of the patient's refusal.

* The incidence of syphilis in this series of cases was greater than indicated by the percentage given as the estimate was based only on one hundred and sixty cases that had Wassermann reactions done, of which twenty-six were positive, confirming other clinical manifestations of the disease. Wassermann reactions were not routinely done on all patients admitted during this period as is now the practice in the hospital.

### Total Operations 64 on 54 Patients

*Major Operations*

| | |
|---|---|
| 1 Mastoid abscess | 1 death. |
| 5 Thigh amputations | 2 deaths, one six months later from tuberculosis. |
| 7 Leg amputations (six patients) | 1 death. |
| Laparotomy for ruptured bleeding, ovarian cyst | Recovery. |
| Thoracotomy: | |
| 1 Lung abscess | Death. |
| 1 Empyema and interlobar abscess | Recovery. |
| 1 Appendectomy and drainage for perforated appendix and peritonitis | Recovery. |
| 1 Intestinal obstruction, incisional hernia | Recovery. |
| 1 Intestinal obstruction, strangulated femoral hernia | Recovery. |
| Supravaginal hysterectomy for bleeding fibroid | Recovery. |
| Partial thyroidectomy, toxic adenoma | Recovery. |
| 1 Cholecystostomy for cholelithiasis | Recovery. |
| 1 Exploratory laparotomy for carcinoma of the bile ducts | Death. |

*Minor Operations*

| | |
|---|---|
| 1 Femoral sympathectomy for Associated Berger's Disease. | |
| 1 Vaginal drainage for pelvic abscess. | |
| 7 Carbuncles | 2 deaths. |
| 3 Cataract operations | 2 deaths. |

Most of the other operative procedures consisted in drainage of abscesses, minor amputations, etc.

### Deaths in Operative Series, 13

*Causes of Death*

| | Period after operation. |
|---|---|
| Coma: | |
| 1 Carbuncle | 24 days |
| 1 Cataract | 8 " |
| 1 Abscess and gangrene of foot, incision and drainage | 2 " |
| 1 Breast abscess | 5 " |
| Uremia and Coma: | |
| 1 Mastoid abscess | 24 hours |
| 1 Cataract | 3 days |
| Uremia—Nephritis: | |
| 1 Amputation at thigh (blood sugar, 125 mg.; urine sugar free, no ketone bodies) | 28 " |
| 1 Carbuncle (blood sugar, 173; no sugar or ketone bodies in urine) | 5 " |
| Other Causes: | |
| 1 Postoperative shock | 12 hours |
| 1 Pulmonary tuberculosis, after amputation | 6 months |
| 1 Pulmonary edema, first stage; operation, lung abscess | 24 hours |
| 1 Pneumonia, after amputation of leg | 8 days |
| 1 Enterocolitis; incision of abscess of thumb | Several days |

ADMISSIONS, JANUARY 1, 1915 TO JANUARY, 1924

203 Cases. Total Mortality, 16.1 per cent

| | |
|---|---|
| Coma | 20 cases |
| Uremia—coma | 3 |
| Total | 23 cases |
| Deaths | 23 |
| Recoveries | 0 |

ADMISSIONS, JANUARY 1, 1924 TO NOVEMBER 15, 1925

122 Cases. Total Mortality, 9.01 per cent

| | |
|---|---|
| Coma | 11 cases |
| Uremia—coma | 2 " |
| Total | 13 cases |
| Deaths | 6 |
| Recoveries | 7 |

No coma cases recovered before 1924. None of the uremia-coma cases have recovered or responded appreciably to insulin treatment in this series.

LESIONS OF LOWER EXTREMITIES REQUIRING OPERATION

| Left. | Right. | Right and left. |
|---|---|---|
| 14 | 3 | 2 |

LESIONS OF LOWER EXTREMITIES (NO OPERATION)

| Left. | Right. | Right and left. | Not stated. |
|---|---|---|---|
| 12 | 8 | 3 | 2 |
| Total | | 44 | |

| Left. | Right. | Right and left. | Not stated. |
|---|---|---|---|
| 26 | 11 | 5 | 2 |

It is seen that coma was the big factor in the cause of death in this series. Of the total coma and uremia-coma cases, 25 were suffering from acute infection of one type or another at the time coma developed. Several of them were victims of pneumonia. Most of the others had infection complicating gangrene of the extremities, carbuncles, abscesses, cellulitis or suppurating ears. Three of the 5 uremia-coma cases also suffered acute infection previous to the onset of coma. Several cases in the nonoperative group were advised to have operation. The patients suffering from carcinoma of the breast and carcinoma of the lower jaw were both operable cases, but refused to submit to operation. Other seemingly suitable operative cases declined and left the hospital against advice, whereas the greater number were totally unfit for surgery, or the

indications in the particular case were not urgent enough to warrant the risk of operation.

Gangrene or gangrenous ulcerations of the lower extremities were by far the most common surgical complications in this group. Arteriosclerosis seemed to be a conspicuous feature in the entire series and was present to a very marked degree in most of the cases showing ulceration and gangrene, and in all of the amputation cases.

It is observed that 19 cases with involvement of the lower extremities came to amputation or operation of one type or another. Several of the cases in the nonoperative group were advised to have amputation and refused, leaving the hospital against advice. A number of the remaining ones in this group, of whom it was thought amputation would eventually be necessary, cleared up with remarkably little loss of tissue under proper dietetic and medical treatment. In addition to diet and insulin therapy, exposure to light and heat (electric-bulb tent) with the use of alcohol locally, for its cleansing and hygroscopic effect, was the treatment usually instituted.

Conservatism, judiciously employed, will yield fairly satisfactory results in gangrene limited to the toes, provided it is of the dry type and not the more rapidly spreading moist type attended with cellulitis and sloughing. At this juncture one should guard against too much optimism, lest the patient become handicapped with the dangers incident to delay. Where there is pronounced obliteration of the main arteries, or if suppuration extends to the sole of the foot involving the tendon sheaths, amputation had best be done. *X*-ray of the vessels is very helpful in determining the degree of sclerosis present.

In the series of amputations there were 5 thigh amputations with 2 deaths. In 1 case death occurred twenty-eight days after operation from uremia, the other death was the result of a disseminated tuberculosis six months after operation. There were 7 amputations of the leg below the knee on 6 patients, with 1 death from pneumonia eight days after operation. One patient had amputation of both legs, about two and a half months apart, from which he made a good recovery. Seven months after the last amputation he had a preliminary iridectomy for cataract. Two months subsequent to this he had a cataract operation and died three days later in uremia-coma.

It is interesting to note, in connection with diabetic lesions of the lower extremities, that involvement of the left foot was much

more common in this series. Being impressed with this fact we reviewed the records of 20 consecutive cases of diabetic gangrene of the lower extremities, occurring at the Jefferson Hopsital, and found them distributed as follows: Right foot, 5; left foot, 12; both feet, 33. Seven of the 13 deaths in the operative series occurred after rather minor surgical procedures. Two of them followed cataract operations (local anesthesia), 1 died of enterocolitis several days after incision and drainage of a badly infected thumb, under Ethyl-chloride anesthesia. Another died in coma five days after incision and drainage of a hemolytic streptococcic breast abscess (nonlactating), following upon a cold—character of anesthesia not stated. One resulted in coma after incision of a gangrenous foot under Ethyl-chloride freezing anesthesia; 2 followed operations upon carbuncles under nitrous oxide anesthesia. Nitrous oxide and oxygen anesthesia was employed in a large majority of the cases and we favor its use routinely in diabetic surgery.

In preinsulin days coma was the cause of death in 70 to 80 per cent of the cases after operation. With the introduction of insulin as a specific in the control of this dreaded complication we are able to carry on surgical procedures with a confidence always hoped for but heretofore never realized. Teamwork is the keynote to surgical success in diabetic surgery. We know of no other condition wherein full coöperation is more essential or where the medical colleague contributes more to surgical success than in diabetes.

Aside from the consideration of increased general risk created by associated disease, such as nephritis, heart disease, arteriosclerosis, etc., the special dangers attending diabetes must be carefully estimated. In cases suffering from acute infection, dehydration is usually an outstanding feature and measures for its correction should at once be instituted. Blood-sugar level is apt to be markedly elevated, and if acidosis is present and coma threatening the $CO_2$ combining power of the blood will be accordingly reduced below its normal level of 55 per cent. We think of the diabetic patient who develops an acute surgical emergency, such as perforated appendix or incarcerated hernia with marked acidosis or threatening coma, as being primarily a medical and secondarily a surgical emergency.

Foster[1] states that patients showing hyperglycemia of over 35 per cent, or a $CO_2$ combining power of less than 40 per cent,

[1] Annals of Surgery, 1920, vol. lxxi.

cannot be expected to survive any operative procedure. He also states: "In order to reduce the risk of operation for the diabetic patient as nearly as possible to the level of the surgical disease for which operation is done, three conditions must be effected: Constant freedom from glucose in the urine, a maximal diurnal blood sugar of less than 200 mg. per cent and absence of acidosis. These conditions may be attained by diet adjustments alone; the use of insulin insures success and shortens the time period required." Dietetic management will embody total dietary restriction, limitation of protein and carbohydrate intake, with maintenance of the fat-carbohydrate balance in order to prevent the accumulation of acetone bodies.

Fifty-seven, or 19.5 per cent, of our patients would not coöperate or left the hospital against advice. Such a percentage is not seen in any other class of patients. Specialization in hospital service and concentrated effort on the part of the dietetic department to satisfy the patient will do much toward gaining their coöperation. Special outpatient clinics educate them in the preparation of their food, the selection of proper foot gear and instruct them as to the prevention of infection. Infection and postoperative acidosis are the important causes of death in diabetic surgery. With these facts in mind, and painstaking coöperation between internist, anesthetist and surgeon, a reasonable mortality rate may be confidently anticipated.

I am deeply indebted to the medical and surgical staff for the privilege of reviewing these cases.

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## DISCUSSION

Dr. Orlando H. Petty: The preparation of Dr. Billings' paper has required a great deal of work. The searching of hospital records back ten years and the arranging of the data recorded are valuable. Yet the time allotted for discussion will permit the discussion only of diabetics requiring surgery since the use of insulin, and we will confine our remarks to the discussion of points which have impressed us as of vital importance in the surgical management of diabetics since insulin was discovered. It is now universally accepted that a diabetic, whether requiring surgery or not, should be placed upon a definite food prescription and his food weighed, that his urine should be sugar-free, his blood-sugar normal and no chemical evidences of ketosis. This ideal condition cannot be realized in those

requiring emergency surgery. If insulin be indicated, and 85 per cent of the cases that we have had referred to us have needed insulin for varying lengths of time, it should be used, the dosage being balanced with the food prescription. Before the use of insulin surgical procedures upon diabetics were usually unsatisfactory and frequently fatal; but by the proper use of diet and insulin the same percentage of success as for nondiabetics in the same age-periods and corresponding physical condition is now assured.

Since Dr. Stoner and I began to use insulin we have had many of each of the following surgical conditions operated upon with a very low mortality: Carbuncles, perforating ulcer of toes with bone necrosis, severe palmar abscess, gangrene of foot and leg requiring amputation, otitis media and mastoiditis, strangulated and simple hernia, intestinal obstruction, general peritonitis from ruptured appendix, ischiorectal abscess and tonsillectomies. The postoperative fatalities of this list, before death, all had a blood-sugar below 150 mg. per 100 cc. of blood (we consider a blood-sugar above 150 mg., either pre- or postoperative, as increasing the surgical risk), with no chemical or clinical evidence of acidosis, and the surgeons agreed with us that other pathologic conditions, including senile changes or acute infections, were unquestionably the cause of death. The surgeons also agree with us that these good results were due to the ready coöperation of the internist and the surgeon. As Prof. John B. Deaver says: "Coöperation between the two is desirable at all times, but at no time more so than in the management of the diabetic. The surgeon, to a great extent, must rely on the judgment and experience of the internist who has made the study of diabetes and its control his own."

The following is the regimen which we have followed and which we most emphatically advocate: The internist or specialist in diseases of metabolism has full charge of and prescribes diet, liquids and medication, both pre- and postoperative, the surgeon having complete charge of the preparation of the field of operation, the technic of the operation and the postoperative care of the wound.

In this way only is the increased risk to diabetics requiring surgery removed. We have divided the preparation of diabetics requiring surgery into the routine diabetic preparation and the emergency diabetic preparation. The preparation of the diabetic, if efficiently done, requires no more time than the routine surgical preparation of the nondiabetic. Routine diabetic preparation should be instituted a few days before operation, as in the ordinary surgical preparation.

*Routine Diabetic Preparation.* Acidosis and blood-sugar estimations are made prior to first meal after admission, and, if acidosis and hyperglycemia are present, administer insulin in proper amounts, estimating insulin effect by blood chemistry within three hours. If the case is a severe one repeat blood chemistry during the night and administer additional insulin if indicated. Give enemas. Diabetics should never be purged. If not a gastric case permit patient to take carbohydrates in liquid form and drink water up to one hour prior to operation. There is no ideal anesthetic for diabetics: Spinal anesthesia can be used; also nitrous oxid-oxygen, ether and, lastly, chloroform; local anesthesia at the line of incision should never

be used on the extremities. Liquids immediately after operation, either by proctoclysis, hypodermoclysis or intravenously, according to the chemical severity of the case. Patient should receive 1000 cc. of liquids every six hours. Subsequent insulin dosage is regulated by the chemical data of the patient. The danger-time for postoperative diabetics is from three to five hours after the completion of the operation. Blood chemistry studies should be made at this time, even if the patient is conscious and apparently doing well.

*Emergency Diabetic Preparation.* The emergency diabetic preparation is as follows: A catheterized specimen of urine is immediately examined for glucose and diacetic acid. If the specimen contains glucose and a definite diacetic acid reaction, procure a specimen of blood for glucose and $CO_2$ estimation, these analyses being done in the laboratory during operation, and then immediately administer 10 or more units of insulin, depending on the glycosuria and the urinary evidences of acidosis before operation.

*Postoperative.* The postoperative treatment of diabetics requiring surgery differs materially from the after-operation treatment of many surgeons. We give carbohydrates and liquids within two or three hours after operation is completed. If oral administration is contraindicated give glucose intravenously and liquids parenterally, for the only way to prevent postoperative acidosis is by administering carbohydrates, liquids and occasionally insulin.

The indication of operations for hernias, acute abdominal conditions and sinuses, including throat, nose and ear surgery, occurs no more frequently in diabetes than in nondiabetics, but operations on the lower extremities are indicated much more frequently than in nondiabetics of the same age, the majority of cases after forty-five years of age having gangrene. Perforating ulcers and phlegmons of the feet occur in diabetics. The gangrene in these cases is usually caused by thermic or mechanical trauma, many cases beginning a few hours after a visit to the chiropodist. I wish I had time to discuss the pregangrenous signs, signs that can be detected months and frequently years before serious conditions develop, yet if properly treated the serious results can be definitely postponed, if not prevented. We have devoted much time to the study of the subject of early recognition of the pregangrenous states in the diabetic's feet and are positive of the above statements. The seat of amputation usually advocated, if more than the toes is involved, is above the knee. Our practice is the following: Place the tourniquet well above the knee; then make incision below the knee; expose the large arteries, incise and examine them and if they have a fair-sized patulous lumen amputate below the knee, and if not, above the knee. By this procedure about 50 per cent of our amputations have been down below the knee with success.

Dr. Billings states that 19.5 per cent of the patients reported would not coöperate and left the hospital against advice, failing to receive the surgical procedures advocated. We have had 100 per cent coöperation. Literally all of our patients submitted to the operation we advocated in amputations, even leaving the place of amputation to our judgment after exploration under anesthesia. We do not claim special persuasive powers, but are

sure such complete coöperation is due to the 100 per cent efficiency of the Departments of Diseases of Metabolism in the Philadelphia General and Polyclinic Hospitals.

Dr. Billings' statement that arteriosclerosis, chronic nephritis, heart disease, syphilis and tuberculosis are more frequent in the diabetic is not confirmed by those studying a large series of cases. In fact, none of these diseases is more frequent in the diabetic than in the nondiabetic for the corresponding age-period.

Dr. Edward S. Dillon: Both Dr. Billings and Dr. Petty have stressed the importance of coöperation between the medical and surgical staffs in taking care of these patients. In the old days it was usually customary to have practically all diabetics with surgical complications admitted to the surgical side of the hospital, even though the only thing the matter was a small carbuncle or infection requiring some comparatively minor surgical procedure. The crisis in these patients is distinctly a medical crisis rather than a surgical one. As Dr. Billings pointed out, practically all these patients die from diabetes and not from infection. The smaller number of surgical cases with the more serious complications, like gallstones, intestinal obstruction and one thing or another of that sort, are perhaps more surgical in nature, as far as danger of death is concerned, than they are medical. In the last few days we had at the hospital a diabetic come in with complete blockage of his large intestine. He had a blood-sugar above 400; he had a low $CO_2$, and it is a question whether sometime ago such a patient would have died from diabetes or whether he would have died from his surgical complication. This man died last night, twenty-four hours or more after a colotomy, with blood-sugar 140 and $CO_2$ 69. Now would he ten years ago have died of diabetes, or would he have died, as he did in this case, from his surgical complication? The surgical cases of diabetes are much harder to take care of, from the point of view of their diabetes, than the nonsurgical. As deleterious as is the effect diabetes may have on infection, even more deleterious is the effect of the infection on the diabetes. That is, the diabetes very rapidly becomes more severe. The patient's tolerance becomes worse and worse, and this may happen very rapidly.

The last slide Dr. Billings showed was of a case at the Pennsylvania Hospital who is still there. When she came in on the first day she had 20 units of insulin and secreted 28 gm. of glucose. After four days she was up to 135 units and still she was showing over 30 gm. in her urine, having been on the same diet all the time. Infections have a bad effect upon the ability of the islands of Langerhans to manufacture insulin. In a like manner, as soon as her infection began to improve her tolerance came back. Only ten days after her abscess was opened her blood-sugar was down to 123 and her insulin was down to 80 and has since gone down to 40 units.

Another patient we had in the hospital last spring had two very severe carbuncles, one on his neck and one on his back. He was in the hospital two months. The infection by the time he left had practically cleared up. For some reason he had to go home. He was then getting 105 units of

insulin a day, but he came to the outpatient department after he left and now he is down to 40, no change having been made in his diet. During all that time his tolerance has been improving.

Another reason why these patients are harder to handle than the nonsurgical is due to the fact that when there is severe infection and toxemia the metabolic rate goes up. They require more calories than the patient who has no fever. If you do not feed sufficient food they will burn their own tissues, that is, for the most part, fat, which is just what you do not want, as acidosis arises from incompletely burned fat. In a patient with a fever you do not actually know how many calories he will need, but you may be sure that he will need more than a patient with a normal temperature. Then again you sometimes have difficulty with these patients in getting them to eat. Now in your nonsurgical cases it is seldom hard to get a diabetic patient to eat. He is willing to eat most anything. But if a diabetic patient has fever and toxemia, he probably will lose any desire to eat, as any nondiabetic would under those circumstances. You may prescribe a diet which in protein, fat and carbohydrate is properly balanced, but if the dietician makes this up with a lot of 3 per cent vegetables he will look at the tray and roll over and refuse to eat anything. That is, the dietician should have been told to make up this prescription with liquid and soft foods and to avoid bulky ones. Various emergencies arise. Suppose you give 25 or 30 units of insulin and the patient refuses to eat the dinner you have prescribed, or suppose he does eat it and promptly vomits it—thus you have given insulin, but there is no food in the patient to balance it. In other words, these patients require very, very close watching from hour to hour. For these reasons and others, I think, it is highly important that medical men should coöperate closely with the surgeons.

# SUBDIAPHRAGMATIC INFLAMMATION *

By ROGER I. LEE, M.D.
BOSTON.

It is with some hesitation that I venture to attack the problem given in the title of this paper, because at the present time our medical knowledge does not permit of any clear-cut classification of the wide variety of conditions concerned. Yet these conditions are by no means uncommon. We have the command of certain instruments, most notably the *x*-ray, which can very definitely help to rescue some of these conditions from their obscurity.

Picqué,[1] in 1910, emphasized the fact that purulent inflammatory processes under the dome of the diaphragm were actually thoracic. He pointed out, what must be obvious on consideration, namely, that in a cross-section of the lower thorax an accumulation of pus, whether below or above the diaphragm, is essentially at the same level. From a clinical viewpoint it makes a vast difference whether the process is above or below the diaphragm. The two processes will have a different origin and will run a different course, and surgical interference, when indicated, may well be quite different. Nevertheless, the clinical signs and not infrequently the clinical symptoms are quite similar, irrespective of whether the abscess in the same situation is just below or just above the thin membrane of the diaphragm. The fact that the signs of this accumulation of fluid are nearly the same has, in general, tended to bring about the inference that the process is above the diaphragm, because that is the more common condition. Moreover, considerable emphasis has always been laid upon the fact that pulmonary and pleural lesions may give rise to abdominal symptoms. For example, it is classical that lobar pneumonia may give abdominal pain, and that when the pneumonia is on the right side the diagnosis between pneumonia and appendicitis may be difficult. The presence of symptoms in the upper chest from lesions below the diaphragm

* Read December 2, 1925.

is not so well recognized, although again we have a classical instance in the pain referred to the right shoulder blade in the case of gallstones. Furthermore, experimental and clinical work have clearly demonstrated that involvement of the diaphragm, particularly the pleural surface, may be associated with upper thoracic pain. As will be brought out in the discussion, subdiaphragmatic processes are not uncommonly associated with those symptoms which ordinarily we attribute to the lungs and pleura, namely, cough and upper thoracic pain.

A further fact, not adequately appreciated, is that in all inflammatory processes within the thorax (and this includes processes both above and below the diaphragm) the diaphragm tends to be high and to be held more or less rigid. This is a protective mechanism—in other words, Nature's attempt to produce rest. Experience in the war showed that in chest wounds, even when the upper portions of the lungs were involved, one usually found the diaphragm rigid and high on the affected side. The same general tendency may be observed to a varying degree in all pulmonary and pleural lesions. Matson[2] has shown that diaphragmatic irregularities occur in acute and chronic conditions in the lungs without involvement of the diaphragmatic pleura. Jackson[3] utilizes the situation and mobility of the diaphragm in the diagnosis as well as in the localization of foreign bodies in the air passages. Actual measurements of the chest will tend to show that the side of the chest which is involved in an inflammatory process tends to be the smaller, and that the diaphragm tends to be high and rigid on that side. It is somewhat striking, for example, to compare the measurements of the two sides of the chest in pneumonia, and even in pleurisy with effusion. I believe it is the general opinion that the affected side is larger in cases of extensive pleural effusion. Simple measurements will readily convince one of the usual contrary findings.

There is likewise a tendency to a high and fixed position of the diaphragm in inflammatory conditions below the diaphragm. The protective position of the diaphragm is always high and relatively fixed. As will be shown later a high diaphragm gives, *per se*, abnormal signs in percussion and auscultation. The usual interpretation of these abnormal signs is some pathology above the diaphragm. In the conditions below the diaphragm one finds the diaphragm held high and rigid to a rather more marked degree than,

as a rule, we find in conditions above the diaphragm. As the process approaches the diaphragm from below one finds a greater tendency for the diaphragm to be held high and rigid. With a mild lesion somewhat distant from the diaphragm the diaphragm may be only slightly involved. In such instances one may find, on clinical examination and by the *x*-ray, that the diaphragm merely lags on the affected side, but can be made on forced inspiration to present an excursion equal to that of the normal side. In those lesions which are in actual contact with the diaphragm one usually finds the diaphragm held fixed.

A further complicating fact in lesions close to the diaphragm is that the diaphragm does not present an insuperable obstacle to the extension of an inflammatory process. In rather rare instances one may find an actual extension of an infectious process from below the diaphragm to above the diaphragm. It is much more common, however, to find that as a result of the infection below the diaphragm there is a response on the part of the pleura, which we designate as the evidence of pleural irritation. In other words, the presence of a sterile, irritative fluid above the diaphragm in subdiaphragmatic lesions is not uncommon. One may readily see the difficulty which is introduced in the diagnosis of these conditions, which simulate a pleural process, when there is actually an accumulation above the diaphragm of sterile fluid which is secondary to the lesion below the diaphragm.

In this paper no attempt will be made to make a complete classification of all of the pathologic conditions below the diaphragm. For example, it is well known that many inflammatory abdominal processes may, under certain condition, have as one of the results a residual accumulation of pus in the recesses afforded by the dome of the diaphragm. The burrowing appendix abscess, the perforated stomach, etc., may result in an undrained abscess below the diaphragm. These conditions are much stressed in the medical literature, and of course give the signs of inflammation below the diaphragm; but the clue to the diagnosis of these secondary processes is, as a rule, found in the primary process. In this paper attention will be paid particularly to those conditions which present lesions which are, in one sense at least, primary, and which are mainly confined to the area under discussion.

Of considerable importance is the appreciation that the large liver and large spleen may encroach upon the thoracic cavity and

are not infrequently mistaken for accumulations of fluid above the diaphragm. It is well known that under conditions, the nature of which is obscure, the enlarged liver and the enlarged spleen may give rise to definite pain, which is usually attributed to the stretching of the capsule of these organs. This pain is by no means a constant finding, nor does it actually parallel the enlargement of the organ. The pain is, as a rule, directly over the organ concerned and may be very definitely thoracic. In a study of a considerable number of cases of "trench fever" in the World War it was found that a goodly proportion complained of pain in the left lower chest simulating closely the pain of pleurisy, and only by careful physical examination or by *x*-ray was it disclosed that the low thoracic dulness was due to the large spleen pushing up the diaphragm on that side. It has been our experience that capable internists not infrequently misinterpret such abnormal thoracic dulness on either side as pleural fluid.

Malignant metastases of the liver and spleen, gummata of the liver, echinococcus cysts of the liver, splenic infarctions and tumors of the kidney and adrenal are some of the other conditions which, under special circumstances, may give a confusing picture. There are certain conditions which cause enlargement of the liver and spleen which may indicate surgical treatment. I refer here particularly to abscesses of the liver, which may be amebic or may be of unknown origin. Obviously the location of the abscess determines largely the signs and symptoms, which may be abdominal, but which may resemble those usually attributed to the lungs and pleura.

Perhaps the most common subdiaphragmatic inflammatory condition that comes properly under the scope of this paper is inflammation around the kidney, which when purulent is called perinephric abscess. The precise etiology of this condition is uncertain. The precise route by which the inflammation arrives in this region is also obscure. It is clear that in a certain proportion of cases this perinephric inflammation is a part of a general pyemia. It may follow insignificant boils. In such an event the causative microorganism is usually the Staphylococcus aureus. There is abundant evidence that other microörganism than the Staphylococcus aureus may be the causative factor of perinephric inflammation. Furthermore, by no means do all of the inflammations in this situation go on to pus formation. Presumably dependent upon the causative microörganisms, the inflammatory process varies here as elsewhere.

Occasionally one may find an abscess of the kidney itself which may extend largely upward and which may correspond to the general clinical picture of a subdiaphragmatic abscess. When the kidney is involved, one expects to find positive evidence from the examination of the urine. However, in that condition known as multiple cortical abscesses of the kidney, which is usually due to the Staphylococcus aureus, one may find a condition somewhat intermediate between the perinephric abscess and a frank abscess of the kidney. In the case of the multiple cortical abscesses of the kidney, in which there is no great extension into the perinephric tissues, one may find the signs and symptoms of the perinephric abscess, but in addition the occasional appearance in the urine of the microörganisms and perhaps pus. This condition is often bilateral, but one kidney may be either exclusively involved or more involved than the other kidney. The acute hematogenous kidney may be roughly described as a somewhat fulminating variation of the above condition.

In addition to the lesions already enumerated, which are characterized by being identified with definite structures, as the liver, spleen or kidney, or with a particular locality, as perinephric inflammation, inflammatory processes may originate (taken in its usual sense) in various situations in this general region. There are instances of subdiaphragmatic inflammation of unknown origin, not only between the dome of the liver and the diaphragm, but also between the spleen and the diaphragm. There are also inflammatory lesions which can be called perinephric only by extremely loose usage, since the tissues primarily involved are some distance from the kidney.

In 1915 I[4] was able to collect a small group of cases which presented a syndrome of signs and radiographic findings. The most plausible interpretation was an inflammatory process of unknown etiology below the diaphragm. These cases did not go on to suppuration, but recovered spontaneously. It would seem, therefore, that nonsuppurative inflammatory processes, while perhaps uncommon, do nevertheless occur in the general anotomical region below the diaphragm. These processes are presumably due to a wide variety of microörganisms, and on the type of microörganism as well as on the situation depends the clinical course.

When inflammation occurs in this situation—that is, within the thorax but below the diaphragm—the course of the process naturally depends largely upon the formation of pus in sufficient amounts as

to require surgical intervention. Sufficient data are not yet available to state positively whether ultimate surgical intervention is a rule or not. It is true, however, that a considerable proportion of these cases, some of which yield pus on exploratory puncture, never come to surgical interference. It is indeed, likely that the typical so-called perinephric abscess (usually due to the Staphylococcus aureus) is merely one end-result of an inflammatory process in this situation. There have been some cases with pus obtained from the region below the diaphragm which showed a growth of Staphylococcus aureus in which spontaneous recovery occurred. A further argument for regarding the perinephric abscess as a convenient term for an end-process is the well-recognized fact of the long duration between the onset and eventual operation. In one series of cases six weeks intervened between the onset of symptoms and the operation.

As has been hinted in the discussion hitherto, a diagnosis of the conditions immediately below the diaphragm is often difficult. From what has been said it must be clear that the key to the situation is the determination of the level of the diaphragm. Experience has shown that it is possible to percuss approximately the upper level of the diaphragm. After a little practise one can arrive at findings which correspond very closely to the *x*-ray findings.

For many years it has been customary to determine the upper border of the liver by percussion over the front of the right chest. The level usually taken is the point at which definite dulness first appears when percussing from above downward. It has been taken for granted, without receiving much emphasis, that this level represents the dome of the diaphragm, and that a wedge of lung tissue extends considerably below, overlaying the liver. Autopsy and *x*-ray studies have confirmed the general accuracy of this finding. For some reason little attention has been paid to the determination of the upper border of the liver behind, or, in other words, the dome of the diaphragm posteriorily on either side. The clinician compares the percussion note on the two sides posteriorily; but, if my experience is any test, he is satisfied with determining the lowest extent of the lung, which, as is well known, is easily demonstrated by the appearance of flatness on percussion from above downward. Differences in percussion between the two sides are generally interpreted as evidence of lesions of the lungs or pleuræ. The *x*-ray, and particularly the fluoroscope, have opened up new possi-

bilities in physical examination. In the normal case the fluoroscope examination will disclose the freely moving diaphragm extending high in the thorax. With quiet breathing, the dome of the diaphragm will reach slightly above the angle of the scapula and, of course, is higher on the right than on the left.

As a matter of practical routine we[5] largely confine our observations to the back; the differences are more easily detected and there is no interference by the heart. The usual procedure is by percussion of each posterior base in turn, moving from above downward, with the patient sitting up. One finds, with quiet breathing, preferably by very light percussion, a level of dulness which corresponds to the dome of the diaphragm. The lower limits of the diaphragm are taken at the place where flatness begins. These levels are normally higher on the right than on the left, on account of the liver. On deep inspiration the dome of the diaphragm should definitely descend and the dulness should, of course, be considerably lower. In case the diaphragm is very high, even if there is no process above the diaphragm, one will find, on quiet breathing, that the level of dulness which indicates the dome of the diaphragm will reach well into the midscapular region. Depending upon the nature of the lesion below the diaphragm, this dulness indicating the top of the diaphragm may or may not descend. It tends to descend somewhat in noninflammatory lesions and in those inflammatory processes not in immediate proximity to it. Not infrequently it will be found that a high diaphragm can be made to descend by forced inspiration. In general, a diaphragm which is high is also somewhat rigid and one finds a diminished excursion on the affected side. It is this high dulness which is apt to suggest to the examiner that the pleura is involved. On the other hand, if both the upper and lower limits of the diaphragm are determined by percussion, and the mobility of the upper limits of dulness is determined, such mistakes may be avoided. Of course, the characteristic fluid line, the displacement of organs and Grocco's sign are valuable.

With auscultation the signs may be confusing, and the signs vary from diminished normal breathing to bronchial breathing depending upon the extent of compression on the lung. Ordinarily one does not expect to find râles. On inspection there is usually some lagging and decreased expansion on the affected side.

These clinical findings are, of course, best supported by the

*x*-ray and particularly the fluoroscope. Early in our experience it was rather surprising to find dulness with definite bronchial breathing at the base of one lung, and then to have the *x*-ray report that the lung fields were clear, that the angles of the diaphragm were also clear and that probably the pathology was below the diaphragm. With our increased experience we now feel that we can usually make our clinical findings correspond to the *x*-ray findings. With the *x*-ray it is important to examine the patient much as he is examined clinically. He is first examined during quiet respiration and the relative levels of the diaphragm are determined. Then the mobility of the diaphragm in ordinary breathing is determined, and finally the mobility during forced breathing. At the same time the lung fields are explored, and the pulmonary angles made by the diaphragm are particularly scrutinized for the evidence of fluid. With the *x*-ray one expects to find a high diaphragm of the affected side with limitation of motion. Sometimes, although the diaphragm is abnormally high, forced inspiration will produce the normal excursion. Certain special features which are familiar to radiologists may be of importance, such as localized irregularities in the diaphragm, abnormal waves of motion, etc. Sometimes the *x*-ray gives us considerable assistance in determining the nature of the process. For example, an abscess due to a perforated stomach may contain air, which may be conspicuously present in the *x*-ray examination. In the presence of the *x*-ray findings described above, the evidence of a small amount of fluid above the diaphragm should not be misleading, since that fluid may occur as a secondary manifestation of the subdiaphragmatic process.

Once the fact is determined that there is an abnormal process below the diaphragm, the part of the diagnosis which concerns the nature of that process is brought into play, and this may be somewhat difficult. In the present discussion we are particularly concerned with inflammatory processes. One finds the usual evidence of inflammatory lesions elsewhere. The presence of fever is fairly constant, but may not be great. Large perinephric abscesses may occur with very little fever. The presence of a leukocytosis presumably depends largely upon the nature of the infecting microorganisms. Those important symptoms and signs of inflammation elsewhere—namely, pain, tenderness and muscular rigidity—obtain in a special form in these conditions. We have learned to consider carefully every statement of the patient in regard to pain in the

chest, back or loins, and carefully investigate these regions for tenderness and rigidity. For some reasons, perhaps because these manifestations are less clear-cut, and also, perhaps, because surgical interference does not seem to depend so immediately upon the analysis of these manifestations, ordinarily little attention is paid to pain, tenderness and rigidity in the thorax. A few clinicians have attempted to insist upon the importance of those signs and symptoms in upper thoracic disease, but their importance has not been generally appreciated by the profession. The amount of pain associated with an inflammatory process below the diaphragm —for example, in the region of the kidney—is variable. It may be rather trifling and may even not be recorded in the history of the case. There are few patients, however, who do not have an appreciable amount of pain, which is usually located near the lesion. Not infrequently the dull pain in the low thorax may be the clue to the diagnosis. Along with pain, sometimes in a different situation from the pain, one can demonstrate, in a large majority of cases, tenderness. In liver abscesses, for example, the tenderness is apt to be directly over the liver, about on a level with the abscess. In perinephric abscesses the pain may be in the lower thorax, in the axillary line; while the tenderness is more apt to be posterior, in the costovertebral space on the affected side. Usually costovertebral tenderness and rigidity are well marked, although, if not definitely looked for, may escape attention. Competent physicians have recorded a negative local history and a negative local examination in some of our cases in which both were definitely positive. One case, although sent into the hospital with the correct diagnosis, was discharged with a diagnosis of constipation, because with rest in bed there was no pain and no fever. Operation, two days after discharge, disclosed a large perinephric abscess. I would like to emphasize here that the symptoms and signs that appear so vague before a subdiaphragmatic lesion is considered, are in reality reasonably definite and do not require the exercise of the imagination.

In the event that there is fluid above the diaphragm as a secondary manifestation of the primary process below the diaphragm, the clinical picture on physical examination may be especially confusing. There is usually $x$-ray evidence that the diaphragm is high and that the fluid accumulation is comparatively slight. The great difficulty of obtaining the fluid is in itself an important clue. The examination of the fluid is important. Data concerning the fluid obtained by

| Case. | Age. | Sex.. | Days from onset disease. | Amount, cc. | Color. | Specific gravity. | Albumin. per cent. | White cells. | P.M.N. per cent. | Lympho. per cent. | Large monos. per cent. | Bacteria smear. | Bacteria culture. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 39 | M. | 21 | 700 | Cloudy | 1.024 | 0.6 | ... | 82 | 18 | 0 | Pn. | 0 |
| | | | 22 | 28 | Bloody | ... | | | 65 | 35 | 0 | 0 | 0 |
| | | | 23 | Few | Bloody | ... | ... | ... | 63 | 37 | 0 | 0 | 0 |
| 2 | 32 | M. | 65 | 30 | Cloudy | ... | ... | ... | 36 | 60 | 4 | 0 | 0 |
| 3 | 26 | M. | 14 | ½ | ... | ... | ... | 510 | 0 | 98 | 2 | | |
| 4 | 40 | F. | 9 | ... | Yellow Cloudy | ... | 3.5 | ... | 65 | 35 | 0 | 0 | |
| 5 | 45 | M. | 21 | 125 | Flakes Yellow | 1.016 | 4.5 | 43,600 | 68 | 32 | 0 | 0 | 0 |
| 6 | 52 | F. | 47 | 50 | Yellow Pink | 1.013 | ... | ... | 60 | 40 | 0 | 0 | 0 |
| 7 | 47 | M. | 45 | 660 | Yellow Cloudy | 1.022 | ... | 800 | 9 | 91 | 0 | 0 | 0 |
| 8 | 24 | F. | 3 | 40 | Yellow | 1.016 | — | 30,000 | 99 | 1 | 0 | 0 | 0 |
| 9 | 35 | M. | 21 | 30 | Yellow Cloudy | 1.020 | | 9,600 | 79 | 21 | 0 | 0 | 0 |
| 10 | 45 | M. | 30 | 30 | Bloody | 1.014 | ... | 700 | 19 | 81 | 0 | 0 | 0 |

P.M.N.—Polymorphonuclear leukocytes.
Large Monos.—Large mononuclear cells, whether classed as blood cells or not.

Lympho.—Lymphocytes.

thoracentesis in one group of 10 cases of subdiaphragmatic inflammation were studied for me by Dr. S. F. Haines, now of Rochester, Minn.; 7 of these cases were proved by operation or autopsy. Bacteriological studies were made of the subdiaphragmatic focus in but 2 cases: In 1 of these Bacillus coli was found and in the other Staphylococcus aureus.

The appearance of the various pleural exudates was not constant, varying from clear yellow and cloudy yellow to bloody. Some contained flakes of fibrin. The specific gravities varied from 1.013 to 1.024. The number of white cells in the fluids was, unfortunately, determined in only 6 of the cases, and in these it varied from 510 to 50,000. In 4 of the cases it was below 10,000. The differential count of the white cells in the fluids showed striking variations. In 6 of the cases polymorphonuclears predominate, being as high as 99 per cent in 1 unproved case, and 82 per cent in a proved case. In the other 4 cases, however, the lymphocytes predominated, in 1 case being as high as 98 per cent, and in another 91 per cent. Two of the cases had low cell-counts in the fluid, 510 and 800 cells per cubic millimeter, respectively, and judged by ordinary criteria were in no way like the fluid expected in an acute inflammatory process. In 1 case pneumococci were reported as present in the smear, but in only one from three separate tappings from that patient; in all the others no organisms were found and the cultures were universally sterile.

These results show a wide variation of secondary inflammatory reactions above the diaphragm. There is but one single constant feature in the cases cited, and that is a uniformly sterile culture from the fluid. The cellular counts are interesting, both because of their wide variation, and because of the great differences noted in the differential cell counts. The cellular picture may be that of a transudate, or of a tuberculous pleural reaction, or it may be that of a mild inflammatory reaction of pyogenic nature. There seems to be no relation between the cellular contents of the fluids examined and the cellular contents of the blood.

These cases seem to show that the cellular formula in pleural effusions cannot be relied upon for as much aid in diagnosis as is frequently given them, especially in cases with atypical symptoms. One of our cases was mistaken for a short time for tuberculous pleurisy. In some cases, however, the fluid findings are distinctly helpful as an aid to diagnosis, more especially in those cases with a

moderate cell-count—around 10,000—and a predominance of polymorphonuclear cells and a sterile culture. The absence of bacteria in the smear and by culture is of great importance. In 1 case the history of two months' duration, particularly with the history of pain relieved by strapping the chest, the presence of fluid of the characteristics given above, caused a note to be recorded by the senior intern that the diagnosis was probably pleural effusion of tubercular origin. However, in this case the *x*-ray showed an unusually high diaphragm on both sides, more marked on the right with evidence of a slight amount of fluid on the right side, with a slight displacement of the heart to the left. The *x*-ray interpretation was a pathologic process below the diaphragm on the right side. Further observation of this particular case showed a tenderness over the right lower chest and increasing pain and tenderness in the right upper quarter in the abdomen. In this case, on account of the confusing picture, the operation was delayed several days after admission, and at operation an extensive purulent peritonitis, which was particularly marked all over the liver, was found. The origin could not be determined.

I want briefly to report 2 cases which show certain illustrative features.

Case I.—A young woman, aged eighteen or nineteen years, had a small boil on her nose. Before this got well she had a pain in the lower left chest and eventually had some fever. She was seen in consultation in another country by an internist of international reputation. She was finally operated upon for thoracic empyema by an equally well-known surgeon, who was very much surprised to find a high diaphragm and only a small amount of straw-colored fluid in the left chest. This wound healed by first intention. The *x*-ray report was "a moderate amount of fluid at the left base, but a very high diaphragm." The culture of the fluid from the chest showed no growth. The *x*-ray interpretation was of a primary process below the diaphragm, but the clinical signs were such that the chest was opened with the expectation of finding an empyema. The subsequent history of the girl showed that the process evidently subsided spontaneously, which in my experience is not at all uncommon.

Case II.—A man, aged fifty-four years, had a carbuncle in the back of his neck. About six weeks later he called a doctor, who told him he had "congestion of the lungs," and he was put to bed for two or three weeks. When he got up again he had a certain amount of irregular fever and pain in his right shoulder. The doctor thought he probably had a small amount of pus in his chest and kept tapping his chest while he was trying to keep

at work. He had some cough, but no sputum. Finally, nine months after the carbuncle and seven months after the so-called "congestion of the lungs," the doctor succeeded in finding some pus on exploratory puncture. He was promptly operated upon for empyema. When the pleura was opened the lung collapsed and there was no evidence of empyema. The wound promptly healed by first intention. He consulted another physician, who told him that he had tuberculosis of the pleura and sent him away for three months. At the end of the year after the onset he was able to go back to work, but he had a good deal of pain in his right shoulder. He was seen two years later, or three years after the onset, when he had the signs of a very high diaphragm on the right. The *x*-ray showed a normal diaphragm on the left, and on the right side there was a very high shadow which was sharply defined and its appearance suggested the outline of the diaphragm. With the *x*-ray no respiratory excursion was found. The upper part of the right lung field was normal. I believe that he had had an extensive, presumably suppurative process below the right diaphragm. It will be recalled that pus was found by exploratory puncture, probably when the diaphragm was pierced. At operation for empyema nothing was found. I believe that the persistent pain in his right shoulder is the referred pain of a diaphragmatic lesion. It is open to question whether, after three years, there is still pus below the diaphragm. In the absence of temperature and leukocytosis, further operation seemed to be undesirable. The early recognition of this condition might have saved many months of complete invalidism and perhaps some permanent disability. We know that there was actually pus present over six months after the onset. Whether there is still a latent process is not determined.

These case reports could be multiplied. They are included for three reasons: (1) The process whether on the left or on the right gives the clinical signs of the ordinary thoracic empyema. In these cases competent internists and surgeons failed to take into consideration that, although the level of the lesion was recognized, it was actually below rather than above the diaphragm. In these 2 cases unnecessary surgery was performed and to the great surprise of the surgeon no pathology was found above the diaphragm. (2) Insufficient weight was given to the radiographic findings. I am far from advocating slavelike adherence to *x*-ray findings. However, the *x*-ray findings were actually confirmatory of the correct clinical interpretation. (3) These 2 cases illustrate the fact that these subdiaphragmatic lesions, even when known to be suppurative, not infrequently in the course of time go on to apparent spontaneous cure.

I believe that there is a considerable group of cases in which data are incomplete and in which such diagnosis as pleurisy with effusion,

thickened pleura, etc., are made which actually belong in this category.

At this time it is not possible to make any positive statement as to what types of cases demand immediate operation and in what types of cases operation may be safely delayed or even avoided. It has been our practice to advise operation with the diagnosis of a subdiaphragmatic inflammatory lesion. Naturally the urgency of the advice varies. It is usually possible to determine the localization of the process, in so far as it is necessary to determine the method of surgical approach. Early operation in 1 case made possible a two-stage transpleural operation which successfully drained the liver abscess. The operation performed at a later date might well have demanded the immediate evacuation of the abscess under undesirable conditions from a surgical point of view. On the other hand, in certain cases of perirenal inflammation an early operation may introduce considerable difficulty in the demonstration of a small localized pus pocket, although abundant evidence of an inflammatory process may be present. It should be remembered that the ordinary course of perinephric abscess is long. The postponement of operation until pus is certainly present makes for an easier operation, but also keeps a potential source of pyemia in the body. Early operation will undoubtedly cause a few cases to be operated upon who would spontaneously recover. In 1 case a positive diagnosis of previous attacks of appendicitis persuaded the surgeon to investigate the appendix. A normal appendix was removed and it was decided to postpone the operation for perirenal inflammation. The infectious process dragged along, always giving rise to hopes that it would subside. However, after a month in a convalescent hospital, operation was finally decided upon because there was still a slight run of temperature, slight leukocytosis and persistence of signs. This belated operation disclosed inspissated pus around the kidney which probably would have taken care of itself. The general evidence, however, is in favor of operation when the diagnosis is established. Furthermore, postponement of operation may lead to disastrous results in any given case.

In this paper I have attempted to stress the existence of inflammatory processes below the diaphragm. I have attempted to point out that these conditions are essentially thoracic in a general sense and are easily confused with thoracic conditions above the

diaphragm. While the diaphragm makes a definite separation within the thorax, nevertheless the situation of these processes is often much the same on cross-section whether they are above or below the diaphragm. I have tried to insist upon the importance of giving careful consideration to the presence of even slight pain and tenderness and rigidity in these conditions. I do not believe that it is necessary to depend exclusively upon the *x*-ray for the determination of the height and mobility of the diaphragm, which is the important clue to the diagnosis. I have tried to describe a satisfactory method of determining the level of the diaphragm, a procedure with has been neglected in physical examination. The *x*-ray is of great value as a means to confirm clinical signs, but its greatest value lies in the fact that by its use we have been able in the past to check up our physical signs and to confirm our deductions, which in the earlier days could only be determined at autopsy. Because in this general region there are different organs and tissues, and because the pathologic conditions vary in their nature, depending largely upon the precise form of the causative microörganism, it is not possible to make at this time any definite classification. It is my hope that in dealing with these obscure conditions I have not made them more obscure in your mind, but in furnishing you with results of our experiences I may have added something to your own experience.

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## DISCUSSION

Dr. William E. Hughes: I am very glad that Dr. Lee's fear of attacking this exceedingly abstruse and very indefinite problem was not sufficient to keep him from doing it. Had he done so we should have missed an exceedingly valuable and interesting paper. Dr. Lee has solved for you many of the difficulties in the diagnosis of a condition which is generally more or less puzzling.

First, the fact that strikes me is that this inflammation, this subdiaphragmatic inflammation, does not necessarily run on to pus. It may be

something that will kill the patient before it has reached that stage or it may resolve before the pus has been formed. That is the first point which makes this exceedingly difficult of diagnosis. You are practically certain that you have some inflammation about the diaphragm, probably beneath the diaphragm; your patient is desperately ill; you advise operation and the surgeon finds nothing. That has been my experience in several cases. Had we waited, possibly pus would have formed. That is the difficulty you have to confront and surmount as best you can.

Then the next point is that inflammation below the diaphragm is inextricably mixed with inflammation above the diaphragm; that is, an inflammation which starts as pleural may become subdiaphragmatic; or, *vice versa*, any inflammation beginning subdiaphragmatic, if it touches the diaphragm, probably becomes supradiaphragmatic.

One point that will help in diagnosis is that the chest case starts out as a chest case, or at least the symptoms and physical signs of chest condition develop fairly rapidly, so that in a little while your doubt has pretty well resolved. In the other case, where it starts below the diaphragm, with very prominent symptoms, you get a slow development of signs above the diaphragm.

Now, of course, the positive signs of any of these conditions, pleural or subdiaphragmatic, is raising of the diaphragm, and I am glad Dr. Lee laid so much stress on the physical exploration of the posterior part of the chest. That is where you make the diagnosis; that is where you go to find absolute heightening of the diaphragm. That is a matter to which attention has been called a number of times. Too much stress cannot be laid on it. It has always seemed to me that the auscultatory physical sign is a trifle more important than Dr. Lee has suggested. That is, where you have primarily a supradiaphragmatic condition you are rather likely to get breathing which is tubular or approaching tubular in the rather earlier stages, and more important is it that you get appreciable changes in the voice sound. This you get rather early in chest cases, and very late or only after secondary empyema has formed in subdiaphragmatic cases.

These cases of which I am speaking just at present are those which arise in direct contact with the diaphragm, for when it comes to perirenal abscess you have a much more easy problem to deal with. The diaphragm is not involved as extensively or as early.

Dr. Astley P. C. Ashhurst: There are two things which have struck me very forcibly in this discussion:

One is the large experience others than myself seem to have had with cases of subphrenic abscess. I looked over my own files and found I have treated only 8 patients in whom I was sure there were subphrenic abscesses. To my mind many of the cases mentioned tonight were not strictly subphrenic abscesses. For instance, many cases of perinephric abscess do not come near the diaphragm. Some of them, if neglected, may in the course of time reach the diaphragm, just as they may reach the abdominal wall and burrow through and discharge externally. But in most cases of perinephric abscess the question of the existence of a subphrenic abscess never arises at all.

The other thing that impresses me about subphrenic abscess is that the diagnosis between empyema and subphrenic abscess is never in doubt when there is a primary empyema, but only when a pleural effusion occurs in the course of a subphrenic abscess. It is like the old question of the differential diagnosis between a supracondylar fracture of the humerus and a posterior dislocation of the elbow: When you are in doubt between the two, the case is one of fracture, not one of dislocation. So if you are in doubt between the diagnosis of empyema and subphrenic abscess, the correct diagnosis is subphrenic abscess, not empyema. When it is a simple empyema, as when there is a simple posterior dislocation of the elbow, there is no doubt about the diagnosis.

Yet in one of my patients with left-sided empyema, following a septicemia with primary appendicular peritonitis, although there was no doubt in my own mind that it was a case of empyema, the late Dr. M. Howard Fussell, to whose service the child had been primarily admitted, was convinced the pus was beneath the diaphragm, and though at my operation he clearly saw that the pus was in the pleural cavity and above the diaphragm, I suspected that when he left the operating room he was of his own opinion still, like most persons who have been convinced against their will.

I take this opportunity of placing on record the following cases of subphrenic abscess which have been under my care: Among the 8 patients there were 4 deaths; 7 patients came to operation—4 before rupture of the abscess into the peritoneal cavity had occurred, with 1 death; 3 after intraperitoneal rupture had taken place, with 2 deaths. These figures, I believe, compare favorably with collected statistics, which show a mortality of 37 per cent for cases treated by operation. The patient under my care in whom no operation was done died of peritonitis. Dr. John B. Deaver has reported 20 cases of subphrenic abscess complicating appendicitis, with 16 deaths, a mortality of 80 per cent.

## Summary of Cases of Subphrenic Abscess

Case I.—January 29, 1902. Female, aged fifty-seven years. Subacute perforation of carcinoma of stomach, forming (*a*) subphrenic abscess beneath left lobe of liver and (*b*) subphrenic abscess in lesser peritoneal cavity. Insidious onset. Death from peritonitis. Diagnosis at autopsy. (*American Journal of the Medical Sciences*, 1902, ii, 629.)

Case II.—December 28, 1907. Female, aged thirty-one years. General peritonitis from appendicitis, with residual abscesses in pelvis, right flank, perigastric and between right lobe of liver and diaphragm. Operation. Death, four days later, from terminal infection. (*Transactions of the Philadelphia Academy of Surgery*, 1911, xiii, 154.)

Case III.—March 23, 1908. Male, aged seventeen years. Appendicitis with diffuse peritonitis. Appendectomy and drainage. Six months later returned with bulging area over lower right ribs. Intercostal transdiaphragmatic incision and drainage. Recovery. (*Transactions of the Philadelphia Academy of Surgery*, 1911, xiii, 156.)

Case IV.—December 22, 1909. Male, aged thirty-two years. Syphilitic. Left lumbar abscess. Opened and drained. Bismuth injections of sinus were coughed up immediately on at least two occasions. Bronchopleural subphrenic lumbar abscess. Recovery. (*Annals of Surgery*, 1923, lxxviii, 99.)

Case V.—August 7, 1914. Female, aged twenty-nine years. Bullet wound of diaphragm and of stomach or left colon. After ten days, signs of fluid at left base; puncture negative. Diagnosis of left subphrenic abscess was made, based on history, fever, thoracic signs, negative puncture and positive Hoover's sign (increased expansion of costal margin on side of disease). Transphrenic thoracotomy two weeks after injury. Death from chronic sepsis, September 15, 1914, nearly six weeks after operation.

Case VI.—November 22, 1914. Male, aged eleven years. Appendectomy and drainage of abscess, November 13 (Friday), 1914. On the ninth day found temperature high, tenderness high in right loin and in front over lower right ribs and at costal margin in midaxillary line. Pitting on pressure. Hoover's sign positive for subphrenic abscess. Lungs negative. Leukocytosis, 27,000, of which 81 per cent were polymorphonuclears. Operation: Subcostal incision in midaxillary line, opening into adhesions. Finger burrowing upward opened abscess between right lobe of liver and diaphragm. Streptococci. Recovery.

Case VII.—September 16, 1919. Male, aged forty-one years. Perforation of gastric ulcer. Operation thirty-seven hours after onset: pus coming from ruptured subphrenic abscess *above* left lobe of liver; perforation 0.5 cm. in diameter on lesser curvature of stomach. Death in three hours.

Case VIII.—October 2, 1921. Male, aged thirty-five years. Operation for symptoms of perforation of stomach. Found a ruptured perigastric abscess with a subphrenic abscess *above* left lobe of liver. No perforation found. Packed. Recovered.

Dr. Lee (closing): I think Dr. Ashhurst brought out very well the reason of my somewhat timorous remarks in the introduction of the paper, and I think brought out the justification of such a paper, because, after all, this subject is rather confusing. It is always very difficult to me, being an internist, when a surgeon finds pus below the diaphragm in reasonable proximity to it, to be sure what structures are involved. I tried to point out that one of the great difficulties in this group of cases is that we cannot make any satisfactory classification and I tried to be as frank as possible in saying so. I think, of course, Dr. Ashhurst is quite right in protesting against the inclusion of pyosalpinx and ischiorectal abscess as subphrenic abscesses. Not even the reader of a paper trying to pad out the statistics would dare to go quite as far as that. However, when the process pre-

sumably goes through the diaphragm, as it did in one series, I think that even Dr. Ashhurst would accept the fact that these were reasonably suitable cases to be included. I do think that there are many more cases than one ordinarily appreciates. I think that there are a good many of these cases which go under other terms. The two illustrated cases happened to come under my subsequent observation after other diagnoses were made, but they are clearly cases of subdiaphragmatic inflammation. These cases simply represent the possibility of a much larger group which are masquerading under other names. I think, as a matter of fact, Dr. Ashhurst and myself are quite in agreement in other things, just as we are in agreement in regard to Litten's phenomenon and also in regard to any group of signs. I tried to point out, as far as my experience goes, there is no pathognomonic group of signs. I endeavored to show the possibility of this condition and to indicate perhaps a new angle for the detection of this condition.

# DIGITALIS INTOLERANCE*

By HARLOW BROOKS, M.D.
NEW YORK.

No other one drug in recent years has received so much attention from pharmacologists and clinicians alike as digitalis. It is now recognized not only as one of our very best drugs, but also one of the very best understood of the drugs of this group, thanks to the enormous amount of work which has been devoted to its study within recent years. This work has been very largely inaugurated, and throughout it has been stimulated, by the splendid example and precept of Arthur Cushny, under whom, as an undergraduate student, I had the privilege of studying. As a result of the teaching and influence of this master I have ever remained a therapeutic optimist, though Cushny was a pharmacologist and not at any time a practitioner. Yet he has always in his researches and publications peculiarly sensed the needs and opportunities of the practitioner.

The persistent and practical work of Cushny and other men of his type, particularly that of a great therapeutist of you own town and of the group which he has stimulated, has done much to preserve an interest and faith in the use of drugs in disease. They are responsible for the recrudescent interest which is now manifest in medicine in the application of drugs to the cure and alleviation of disease. Therapeutics had almost become a taboo subject in many medical societies; it had become almost scientific sedition during the now-rapidly-waning period of therapeutic nihilism to mention drug treatment in almost any disease. Hence the rapid growth of commercial proprietary drugs in Germany and America.

Happily digitalis itself, originally used empirically, has been one of the outstanding pillars of our persisting therapeutic faith. Even the most pessimistic nihilist can hardly observe the miraculous effects of digitalis in auricular fibrillation and in many other forms of

* Read December 2, 1925.

cardiac deficiency without feeling the very basis of his pessimism crumble away.

Perhaps it was quite natural that Cushny, who was a Scot, should have early interested himself in digitalis, for it was another Scotchman, Withering, who published, in 1785, the epoch-making paper, "Account of the Foxglove." Withering, it seems, had had his attention first attracted to foxglove by an old lady who had observed its beneficial effects in "dropsy." After this experience he lost no opportunity to test out the drug in various disturbances of the heart. Withering persisted in his studies, and he had what must have been the tremendous satisfaction of seeing digitalis introduced into the Edinburgh *Pharmacopœia* in 1783. He first began its use in 1776, a date which is still of some other interest to Philadelphians as well as to the citizens of this country at large.

It is, of course, generally recognized that digitalis had been previously used for an indefinite period of time by uncivilized peoples. We know, for example, that our Indians used it and applied it quite correctly, probably long before they made the acquaintance of the white man. The Navahoe uses it today in its crude form, but with good effect in properly selected instances. It might be well for us to consider more seriously still other medicinal substances which primitive peoples have employed empirically. At least we owe the Indian an acknowledged debt for digitalis, cascara and quinine. There are still other useful drugs of which he at least knew as much as we.

In this short paper I have chosen to speak for a few moments only on the subject of digitalis intolerance. I do not speak as a pharmacologist, which I am not, nor as a pharmacist or chemist, which I also am not, but as a mere practitioner.

Every physician has encountered cases in which digitalis seems to be indicated, but in which the drug could not be used sufficiently long or in large enough doses to produce the desired and expected result. In some of these instances, perhaps, the reason for this intolerance has been apparent; in others not. In some patients the drug in its therapeutic degree of action is, for some reason, inert: Note its limited effect in hyperthyroidism and in the degenerated muscle of diphtheria. In others it is apparently therapeutically effective, but cannot be maintained long enough or in sufficient dosage to produce its desired effect.

In modern practice we have largely tended to simplify our drugs;

at least here in America. Notwithstanding the efforts of many drug companies, digitalis is now used almost universally in the form of the tincture. There are many reasons for this preference for the tincture; we do not need to go into them here. Most of us speak of digitalis dosage in the calibration of the tincture. I find in many hospitals that it is used practically universally, except for hypodermic or intravenous purposes. This tendency can be carried too far.

In several cases under my observation I have found that other of the standard preparations are better tolerated, though in most cases the tincture entirely suffices. I have seen, for example, cases in which the infusion was carried successfully in larger unit doses than the tincture. In more than a few patients I find that the powdered leaves or some of the similar preparations (there are numerous such on the market) will be borne in sufficient unit-dosage when the patient is intolerant to satisfactory doses of the tincture. The leaves, prescribed with sodium bicarbonate combined with quinine or given with various digestives, may occasionally be also very effectively employed when the tincture is not well borne.

Briefly, I believe that there is a real need for all the standard preparations of the drugs. We must not assume because the patient fails to respond to certain forms of digitalis, or will not tolerate it in one preparation, that therefore it is impossible to satisfactorily use digitalis in that particular case.

I find also that in certain individuals a simple disguise of the drug in some menstruum, usually an inert substance, permits it to be given to its full effect. It may be in these instances that long association of the smell and taste of the drug with sickness and discomfort, perhaps with the nausea which is almost always the first indication of the point of dose tolerance, may so disgust the patient that he is unable to take the drug, or he thinks that he is, which in practice if not in the laboratory amounts to the same thing. Digitalis may then be given with good result in some aromatic syrup, in the elixir aromatic, in port-wine or some other alcoholic. Perhaps the patient does imagine that the digitalis makes him sick taken simply diluted in water. It really amounts to the same thing if we will take the trouble to disguise it to make it palatable for him. Digitalene, digalin and other similar concentrated preparations are also sometimes taken satisfactorily where the more usual forms are not tolerated in effective dosage.

In a good many cases where the tincture is given by mouth in the usual satisfactory dosage, especially in gastrointestinal and hepatic disease, it causes early nausea. This may be often entirely corrected by associated symptomatic treatment of the gastrointestinal symptoms—by hydrochloric acid in small doses, by sodium bicarbonate or other alkalies and so on. Again it will be found that some patients will show better toleration if they are given one massive dose, properly administered, daily or on alternate days, while others show much better effect if the administration of the drug is extended by the use of smaller doses given more frequently.

Nearly every clinician has found that better digitalis effects are secured in cases demanding long-continued administration if the drug is given in broken periods, say three days out of each week, one week out of each month and so on. Administered in this way the prolonged effect is usually much more easily attained without the production of symptoms of intolerance. The "drug disgust," which more than infrequently terminates with sensitive patients possibility of carrying on with a prolonged course of necessary digitalis treatment, is obviated in the same way.

Most of us have attempted to calibrate our doses of digitalis by the rules laid down according to body weight by Eggleston and other pharmacologists. In the main this works out in a fairly satisfactory way, especially when rapid digitalization is desirable. All practitioners have long since discovered that there is no way in which we can determine the amount of drug which is absorbed, no matter how punctiliously we may calibrate the amount given. No doubt, where digitalization by the rapid method appears advisable, as is the case in a good many but by no means all cases, the determination of the dose by the weight of the patient is a very useful guidance; but one should not attempt to rely on this rule except in a very rough and general way. Many years ago Cushny taught his students that digitalis should be given until digitalis effect was produced. In this day of much more carefully standardized preparations and much more effective ones the rule still holds for the utilization of the drug in actual practice. What is wanted is digitalis effect, and until this has been attained, no matter how much may have been given, enough has perhaps not been utilized by the body tissues. There is but little danger of overdosage unless the drug is given in tremendous dosage, carelessly or ignorantly. The early signs of saturation are very manifest, and its early stages are

not dangerous but mildly disagreeable. I have in all my life seen but one case definitely killed by digitalis.

The manner of administration of digitalis is often of primary importance. With such a drug, where in a large percentage of cases the use must extend over long periods of time, administration by mouth is naturally the favorite and most obvious method. Under normal conditions it is thus quickly absorbed, and given in modern dosage digitalization can thus be very quickly effected. Except in sensitized patients, the drug is ordinarily sufficiently well tolerated to permit of efficient dosage by mouth. Furthermore, most of the preparations designed for administration through this channel are now very well standardized and effective. When need be, as mentioned, the drug may be disguised.

There are, however, cases when it cannot be given by mouth for one reason or another, not so infrequently because so given in anything like effective doses it causes early nausea. It is true that this can be overcome in a good many instances by some of the methods mentioned, but there still remain instances where mouth administration is not satisfactory. My first appeal in cases of this kind, especially when the mouth administration is prevented because of the gastrointestinal irritation, nausea and vomiting, is to consider the use of the drug by rectum. I am well aware that pharmacologists tell us that the production of nausea and vomiting in digitalis is through central influence; but all who have taken the drug themselves, or who have carefully studied its administration in large numbers of patients, realize that there is also a nausea and gastrointestinal irritation in very many cases which occurs, as Cushny indicates to be possible, by the direct effect of the drug on the gastric mucosa. This is entirely avoided by administration by rectum. Here nausea is produced usually only when saturation has taken place and through central effect.

Perhaps it is hardly correct to speak of the rectal administration of digitalis when I really mean that the drug should be introduced in some bland menstruum into the sigmoid. For this purpose the patient may be quickly instructed so that he can give the drug himself. A catheter attached to an ordinary glass syringe is introduced 8 to 10 inches through the rectum and the injection then made. I ordinarily employ the tincture also for this purpose, usually in ʒ j or ʒ ij of starch water. There are patients, however, in definite imperative need of digitalis who are unable to tolerate

the drug given in this manner, sometimes because of sensitiveness to digitalis. I have seen nausea appear in such cases from the giving per sigmoid of no more than 30 gm. per day for two doses only. In some instances, because of local disease, this avenue is closed.

Intramuscular and subcutaneous administration are perfectly practical, of course, in instances where a nurse is in immediate attendance on the patient or when the physician can see him at frequent intervals. This method has many disadvantages, among them the outstanding fact that I know of no preparation designed for this method of administration which compares in efficiency and accuracy of standardization with the tincture. Nausea and vomiting generally occur quite as quickly by this method as when the drug is introduced by mouth. Pardee believes as a result of his studies that these preparations and this method of administration are much less prompt in effect than dosage by mouth.

It is occasionally found that patients will not bear the administration of digitalis in any form in sufficient dosage or sufficiently long to give a digitalis effect, no matter how ingenious one may be in the manipulation of the drug. It is generally known that strophanthus ordinarily is more irritant to the gastrointestinal tract that the digitalis preparations. There are, however, certain cases (I do not know how to foretell them, however, except by experiment) which respond much more satisfactorily to strophanthus than to digitalis in any form. Occasionally it will be found that strophanthus will act very happily in cases which have for some reason ceased to respond to digitalis. Ordinarily I first appeal to the tincture of strophanthus, but there are other cases in which a satisfactory preparation of strophanthus acts far more satisfactorily. It is a stock text-statement that it is dangerous to introduce strophanthin, especially intravenously, in cases which have received digitalis in large dosage, even without effect. I was inclined to discount this statement when I found that some instances which had failed to respond under digitalis to brilliantly compensate under strophanthin. Then came three instances in which a single dose of strophanthin so given produced a death so nearly immediate and so strikingly characteristic that there can be no remaining doubt in my mind but that the caution is very well based. I now use it only when digitalis has been discontinued for three or more days, and when all the toxic effects of digitalis have disappeared.

We all know that convallaria, while of the digitalis group, is usually of very much less therapeutic value and very much more likely to produce toxic and irritant symptoms than digitalis. It is not ordinarily comparable in its most satisfactory cases with a usual digitalis effect. I have, however, proved to my full satisfaction that there are instances that respond much better to convallaria than to digitalis. I have used in my experiments only the tincture. Delafield, whose wise teachings are far from forgotten in New York, urged convallaria, especially in those instances in which the right heart appeared to be especially at fault. He asserted that it had a specific action in such instances. In so far as I have been able to find, this theory has not been substantiated by any pharmacological studies, nor have my clinical observations tended to support it. On the contrary, the Lamberts, Samuel and Alexander, still use the drug successfully in such instances, and I must admit that they get results. I do not believe that we are prepared to discard even convallaria.

Three years Donaldson and myself made a study on our service of the toxicity of digitalis administered to the point of full tolerance, with the view of determining what was the first evidence of the end of digitalis tolerance. Very briefly stated, we arrived only at the well-established conclusion that nausea and vomiting are the first indications. Heart-block was a very exceptional first evidence of digitalis toxic effect. It occurred only in instances which we believed presented preëxisting bundle defects, and we believe that, therefore, the therapeutist is justified in perfect safety to persist in the use of digitalis at least up to the point of nausea and vomiting.

During the past winter the members of my staff at the City Hospital have been making a clinical study of methods of combatting the nausea and vomiting in cases which developed this symptom before real digitalis therapeutic effect was produced, and yet in cases in which full digitalis effect was very desirable. We have met with some very interesting and hopefully suggestive results.

The sedatives have been most beneficial in this regard. Morphine has acted in a perfectly satisfactory way in a few cases. The best results were reached when the morphine was given in small doses. Other instances had relief from nausea and vomiting when the digitalis was administered by the sigmoid and gastric lavage performed once daily, usually with a mild alkaline solution. Some cases were permitted a continuation of the digitalis to its desired

effect when sodium bicarbonate was given in fairly large doses. Others were relieved when the laxative preparations of magnesia—the sulphate, oxide and the milk of magnesia—were given. Still other good results have been reached by the giving of the bromides, usually by rectum. The same benefits has also followed the employment of chloral hydrate and similar sedative drugs. By such means we have been enabled to give our digitalis to its desired effect in several cases which demanded this result but which were entirely unable to maintain a sufficient dosage without this assistance.

By far our most satisfactory effects have been reached, however, by the combination of cocaine administration with the digitalis. Very small doses of cocaine usually suffice, and in most instances the manner of cocaine administration has apparently not been very important. We have given it intramuscularly, by stomach and by the sigmoid. Usually gr. $\frac{1}{10}$ has sufficed. It acts most satisfactorily when the cocaine is given by mouth, well diluted, or by rectum about an hour before the single sufficient daily dose of digitalis was given. We are very partial to giving the cocaine by rectum and following it in one hour by our single daily dose of digitalis given by the same avenue.

Our first and most striking case illustrating this point was a young woman, aged twenty-six years, who had an original double mitral endocarditis with great subsequent dilatation, auricular fibrillation, tricuspid incompetence, edema of tremendous grade, enlarged liver and spleen and utter misery. She had remained in this condition for two years, passing from hospital to hospital. She utterly failed to respond therapeutically to any or either of the digitalis group of drugs administered in any way. Each dose was followed by almost immediate vomiting, no matter what form or in what manner the digitalis or strophanthus was given. Uncontrolable vomiting would appear within two hours after the giving of any therapeutic-sized dose of digitalis or strophanthus. Rest, Karell diet, saline laxatives and all substitute and adjuvant measures were tried by ourselves and by other hospitals entirely without effect. No results whatever were reached by us until we preceded digitalis by gr. $\frac{1}{5}$ of cocaine given by rectum. One hour later tincture of digitalis ʒij was introduced into the rectum. No vomiting or nausea appeared. This was repeated daily with no bad effect. Within two days the patient developed a tremendous

diuresis and within a week she was free from her edema, able to sit up. She presented as typical and beautiful a picture of digitalis effect as I have ever seen. Within a month she was walking about the ward, assisting in the routine work, and within three months she was discharged from the hospital fully compensated. Several times we experimentally gave the digitalis without the cocaine, always with severe vomiting within a few hours. During the last period of her stay in the hospital the digitalis was given but once weekly, as is our custom of periodic dosage, but she was never able to take it without the cocaine, though we still found a perfect effect when the cocaine was reduced to gr. $\frac{1}{10}$. Similar, if less striking, results have followed this method in other cases.

My purpose in presenting this somewhat incoherent paper has been to emphasize, especially for the younger men among us, the value of experimental studies in materia medica; to show the need for different forms of the same drugs, to encourage once more a polypharmacy worked out in the wards and not in the laboratories of the manufacturing proprietary pharmacists. Finally, I wish to illustrate, on this one hundred and fortieth anniversary of Withering's paper, the still existing value of studies in empirical medicine.

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## DISCUSSION

Dr. Horatio C. Wood, Jr.: It comes to me as a breeze off the ocean on a hot summer day to hear somebody get up and talk about the value of materia medica in these days of disregard for materia medica. I think it was Dr. Hare who remarked, in discussion at the College some months ago, that the real function of the pharmacologist was to confirm and explain the discoveries of the clinician, not to discover new remedies. That there is a good deal of truth in this is well illustrated by digitalis. Some seventy-five years ago my great uncle, Dr. George B. Wood, wrote in his textbook: "Some believe digitalis is a cardiac stimulant, but I hold it is rather a sedative than a stimulant." It was some time about 1870 that Sir Lauder Brunton published his epochmaking paper based on the study of digitalis in animals, which for the previous generation settled the question of digitalis as a stimulant. When I was a student we were taught long arguments to show how the increase in the tone of the ventricle diminished the leakage back through a diseased mitral valve. Now we know that Brunton's conclusions were erroneous, because they were based on toxic doses. Pharmacologists have in this case rather led the clinicians astray than been of any real value to them.

There is very little that can be added to Dr. Brooks' paper because he has covered the subject in so admirable a manner, even if he does claim incoherency for it. There are one or two points, however, that I think might be emphasized. In the first place, as to the cause of the nausea: I think it is well demonstrated that the emetic principle of digitalis is digitoxin and the other glucosides which affect the heart; therefore, it is ridiculous to hope to find a preparation of digitalis that shall not be nauseating and shall be efficient. I do not say that it would be undesirable to find such a preparation, but we may rest assured we are not going to find such a preparation. I do not think it is finally settled, but I am inclined to the view of Dr. Hatcher that the nausea is a reflex irritation of the emetic center from the heart, and that is the reason why the two tolerances go together. I could not quite make out from Dr. Brooks, when he spoke of the nausea as a dosage limit, if he was speaking of those cases in which he attempted to control the nausea with other drugs. I should imagine it would be possible to depress the emetic center so that it would not feel the reflex from the heart. It would seem if he did this he would be treading on rather a dangerous ground.

I want to say one word more in connection with infusion of digitalis: That is, the new *Pharmacopœia*, which will become official on January 1, 1926, has changed the method of preparing infusion of digitalis. In the past, although it theoretically represented 1.5 per cent, it was in reality somewhat less, because the method of making it did not completely extract the drug, but by new pharmacopeial manipulation the process has been improved, and those of you used to giving the infusion in certain doses should be a little careful about the dose of the infusion you employ.

Dr. George W. Norris: I would ask Dr. Brooks whether he has ever, and if so how often, satisfactorily controlled auricular fibrillation by means of convallaria?

Dr. Brooks (closing): I think that Dr. Wood misunderstands me; perhaps I was "incoherent." I know that one can control by drugs the symptoms which arise in many cases of poisonous doses of digitalis. One can depress the center—that is, stop vomiting—by drugs in instances in which without this assistance digitalis may not be given in suitable dosage.

From my experience I think that it is very difficult to produce death from digitalis poisoning. I have seen but one instance of death from digitalis poisoning. It is easily possible to confer great benefit on many cases, however, by massive digitalis dosage; the great probable benefit is well worth the improbable risk of doing harm to the patient in those demanding digitalis effect.

Dr. Norris' question is very well put. He asks if I have been able to control auricular fibrillation by convallaria? I have not. I am not very hopeful of ever reaching this result with convallaria, though I have seen undoubted benefit occur in some instances which had failed under digitalis. The Lamberts, Sam and Alexander, employ convallaria after the teaching of Delafield, and they report excellent results from it. Delafield believed convallaria to be particularly beneficial in defective action of the right heart.

# THE RELATION OF MECHANICAL AND ELECTRICAL PHENOMENA OF MUSCULAR CONTRACTION, WITH SPECIAL REFERENCE TO THE CARDIAC MUSCLE*

THE MARY SCOTT NEWBOLD LECTURE
LECTURE XV

BY PROFESSOR W. EINTHOVEN
UNIVERSITY OF LEYDEN, HOLLAND

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THIS lecture was also delivered by Professor Einthoven in identical form as The Harvey Lecture before the Harvey Society in New York.

It can be found published in full in "The Harvey Lectures, delivered under the auspices of the Harvey Society of New York, under the Patronage of the New York Academy of Medicine." Volume for 1924–1925, Twentieth Series.—EDITOR.

* Read December, 1924.

# THE NATURE AND MODE OF REGULATION OF GLOMERULAR FUNCTION.*

## The Mary Scott Newbold Lecture

## Lecture XVI

By A. N. RICHARDS, Ph.D.

(From the Laboratory of Pharmacology of the University of Pennsylvania Medical School.)

The literature of investigations of the function of the kidney reveals two distinct types of work. In one the kidney has been studied as one unit in the aggregate of organs which makes up the animal body—a unit upon the normality of whose function the welfare of the rest of the body depends. In such study the reactions of the kidney as a whole to changes in the conditions under which it works have been determined and expressed in terms of change in amount and character of urine eliminated. Such study has had the highest importance in the development of conceptions of the rôle which the kidney plays in the maintenance of that constancy of composition of body tissues and fluids which is essential for health; and it has directly aided the physician in practical problems in which he is required to detect and to evaluate abnormalities of renal function encountered in disease. For the purpose of such study it is not at all inconsistent with the requirements of scientific inquiry to regard the kidney itself as a unit, to speak figuratively, as a sieve with blood pouring into one opening and urine issuing from another—a sieve whose inlet, outlet and size of mesh are exquisitely adaptable to the necessities of the organism as a whole. Such expressions as "renal permeability," "renal threshold" are current illustrations of this implication.

In the second group of investigations are to be found those studies of kidney function in which effort is made to analyze the

* Read April 21, 1925.

fashion in which the kidney performs its work. The basis of these efforts is recognition of the fact that the kidney, far from being a homogeneous structure, is a compact assemblage of millions of minute structures, and each of these, in turn, is composed of a number of highly differentiated parts; and that these minute parts are functionally adjusted with incredible nicety not only to each other but to the activities of the rest of the body as well. It is the aim of the student who wishes to analyze the function of the kidney on this basis to cultivate sufficient imagination and skill in experimentation to accomplish the identification and separate study of the functions of each different structure of which the kidney is composed, to the end that eventually he may obtain a conception of the workings of the kidney as a whole which includes an understanding of the contribution which each element of the kidney supplies. The results of such study are not apt to yield direct and immediate assistance to the physician in the solution of practical problems; but if they lead to sounder conceptions of the fundamental processes of kidney function they can hardly fail to furnish the basis for greater discernment and better judgment in practical tasks which concern it.

The work which I propose to describe belongs in this second category. It has been proceeding for ten years in the laboratory of which I am in charge and it is still in progress. The work would not have been possible except for the collaboration of a number of colleagues whose names I shall mention in appropriate connections and to whom the highest credit should be given.

The title of this account, "The Nature and Mode of Regulation of Glomerular Function," intimates the restriction of our discussion to one small part of the kidney. I think that we have enough information concerning glomerular function to warrant this; and I wished to make this choice of title implicitly express my conviction that until we can arrive at a reasonably accurate understanding of the part played by glomerular structures in urine formation, our footholds for progress toward elucidation of the function of the renal tubules are insecure. The literature of renal physiology contains an enormous amount of speculation, owing to the fact that intricacy of structure has made unambiguous experiment difficult. When we shall have designed and made unambiguous experiments on the glomerulus of such sort as to remove or lessen materially the necessity of speculation concerning its function we shall surely

find that the speculative element in a consideration of tubular function is diminished.

Bowman,[1] in 1842, was the first who satisfactorily demonstrated that the tuft of capillaries which we call the glomerulus is actually inserted into the end of the tubule, the modified wall of which is expanded to form the capsule in which the tuft is enclosed. Hence the intracapsular space is the beginning of the lumen of the renal tubule. He advanced the view that fluid leaves the blood as it passes through the glomerular capillaries, and that this fluid, washing the inner surface of the cells composing the tubule, carries away the products of their secretory activity. He conceived the glomeruli to act as an automatic "sluice" by which water, salts of which the body was not in need, and many foreign substances were eliminated. Experimental evidence supporting the correctness of this view that fluid issues from the glomerular capillaries was supplied by Nussbaum[2] in 1878; indirect evidence was adduced by Brodie and Mackenzie[3] in 1914. But in 1922 and 1923 W. N. F. Woodland[4] published a series of studies of the frog's kidney which led him to the view that the glomerulus has nothing whatever to do with the actual production of urine but acts rather as a pressure-reducing valve in the circulation to the tubules, by which he conceives the entire urine to be secreted. It is not necessary to enter upon a detailed critique of Woodland's work. But since the question raised is fundamental to the discussion which I am beginning, it must of necessity be answered. The answer which, I think, completely controverts Woodland is found in an observation by Wearn[5] made in our laboratory. By methods presently to be described, we taught ourselves to penetrate Bowman's capsule in the frog's kidney with a very finely pointed capillary pipette. By this means fluid from the capsule could be collected continuously for many hours. When blood ceased flowing through the glomerular capillaries fluid ceased rising in the capillary tube, though interruption of glomerular flow in the frog does not entail interruption in flow through vessels supplying tubules. In one experiment, by accident rather than by design, the opening from capsular space into the lumen of tubule was closed by a droplet of mercury injected into the capsular space. Accumulation of glomerular fluid in the pipette, previously slow and unsatisfactory, now became rapid. This observation demonstrates in conclusive fashion the correctness of Bowman's assumption and the fallacy of Woodland's.

Having proof that fluid which is eventually to become urine leaves the blood during its passage through the glomerular capillaries, we may take up the question of the nature of the responsible process involved. Examination of the arrangement of glomerular capillaries in contrast with capillaries in other areas shows certain definite differences. In the glomerulus a single arteriole, the vas afferens, breaks abruptly into a number of capillaries (in the frog three primary and six secondary branchings; in mammals, from the drawings of Bowman, many more). In the abrupt transition from afferent vessel to glomerular capillaries the cross-section of the vascular bed increases many times; no such abrupt increase is found in other vascular areas. In the glomerulus the capillaries reassemble into the efferent vessel, smaller in diameter than the afferent; whereas in other vascular areas the efferent veins are larger than the arteries. Further, the length of the smaller arterioles leading to the glomerular system of capillaries is less than is length of the arterioles leading to the capillaries in other tissues, and as a result the head of pressure in blood reaching the glomerular capillaries must be higher than that in blood reaching other capillary areas.

Such considerations as these led Ludwig to the view that the blood-pressure in the capillaries of the glomerular tuft is higher than in other regions; and that in consequence a protein-free filtrate is pressed out of the plasma through the capillary wall.[6] This is the filtration theory. It received support from experiments in which a parallelism was shown to exist between urine formation and renal arterial blood-pressure. After general acceptance for some thirty years it was effectively attacked by Heidenhain,[7] on three chief grounds: (1) That certain dyes, injected into the circulation, appear to be eliminated by the tubules and not by the glomerulus, as judged by the appearance of sections of the kidney made after death; (2) that partial obstruction of the renal vein—a measure conceived to be capable of increasing pressure in the glomerular vessels—does not increase urine; (3) that the amount of glomerular filtration necessary to unload from the blood the amount of urea which is eliminated daily by the kidney was incredibly large when compared with his estimate of daily volume of bloodflow through the renal vessels. These apparently insuperable objections led Heidenhain to substitute for the filtration theory an hypothesis which ascribed to the epithelium known to envelop

the glomerular capillaries a power of causing the withdrawal of a fluid from the blood passing through these capillaries. Ludwig, in advancing the filtration theory, was obliged to attach to it a theory that reabsorption occurs in the tubules. Heidenhain, denying filtration, saw no need of a reabsorptive process, but saw in his results evidence of a secretory process in tubule cells. Following Heidenhain's work faith in the filtration hypothesis diminished. It was revived, however, some twenty-five years later by the work of Starling,[8] in which was demonstrated the striking coincidence between the osmotic pressure of the plasma colloids and the values which he was able to assign for the minimal glomerular capillary pressure at which urine was formed. As late as 1910, however, opinions held by competent students of kidney function were divided on this question.[9]

The question is one which is of a great deal of interest to one who is obliged to interpret the diuretic action of drugs, for the reason that the interpretation of such action can be no more convincing than is his conception of the processes which the drugs affect. The beginning of the experiments which we have made was undertaken for the purpose of discovering whether the secretory theory of renal function was better suited to explain the action of caffein upon the kidney than was the filtration theory. An apparatus was made by Drinker and myself,[10] by which blood could be passed through the living kidney of a rabbit *in situ* in a manner which closely resembled that in which blood is pumped by the animal's heart, but with one difference, that the mechanical pump which we arranged was constant in its output regardless of the state of dilatation or constriction of the vessels through which the blood was pumped. Plant and I applied the apparatus to the study of the action of caffein on the rabbit's kidney *in situ*.[11] It was our thought that if caffein were not capable of producing diuresis under conditions which did not permit alteration in bloodflow through the kidney, the conclusion would be justified that the normal diuretic action of caffein is a vascular one. The result showed, however, that caffein was able to produce marked diuresis under the conditions stated, and for a time, therefore, we were inclined to regard our results as in harmony with the secretory theory of urinary production.

But during these experiments it became obvious that we had in our hands a method for an attack upon the problem of the nature

of the forces which are responsible for urine formation more direct than any previously available. We had found it possible to maintain the activity of the living kidney with an artificial and controllable circulation of blood through its vessels. It was easily possible to vary the pressure within this artificial circulation without at the same time necessarily influencing the volume of bloodflow through the organ per minute. Hence it appeared possible to test the validity of the filtration hypothesis by keeping all recognizable conditions constant with one exception, viz: pressure of blood flowing through its vessels. The experiment was made many times with the uniform result that under conditions which completely prevented an increase in bloodflow through the kidney, any considerable increase in pressure was associated with a parallel increase in urinary output.[12] The means by which pressure was raised in these experiments were stimulation of the splanchnic nerve, injection of adrenalin into the circulation and partial obstruction of the renal vein. None of those agencies commonly causes diuresis in the intact animal, because they all lessen the bloodflow in the renal vessels. In our experiment bloodflow was not diminished because of the efficiency of our pump, and the relationship between renal blood-pressure and urine flow was clearly revealed.

For the first time indubitable evidence was gained that alterations in pressure alone in the renal circulation were responsible for alterations in urinary output, and the experiments may be regarded as the most direct evidence in support of the filtration hypothesis available at the time they were made. By a similar method Dreyer and Verney,[13] in Starling's laboratory, have recently obtained similar results.

My reason for having introduced into this discussion an account of these old experiments is that their results, decisively confirmatory of the observations and reasoning of Ludwig's followers and decisively refuting one of Heidenhain's chief objections, gave us a conviction of the essential soundness of the filtration hypothesis which subsequent experience has not shaken; and they provided suggestions for the design of further experiments which otherwise would not have occurred to us.

In the experiments which immediately followed these, evidence was obtained bearing upon the regulation of glomerular function. These I shall presently describe. A further outcome has been the

design of two series of experiments which bear, the one indirectly, the other directly, upon the nature of the glomerular process. This work was based upon the observation which had been made by Dr. Schmidt and myself, that it is possible to apply, after the manner of Krogh, methods of direct illumination to the kidney of the frog with the result that the glomerular vessels and the blood flowing through them becomes easily accessible to direct microscopic vision. Through the work of Barbour, Kite and, more recently, Chambers[14] methods have been developed for microdissection and microinjections. Professor Chambers, of Cornell, has been able to make capillary pipettes of such extreme fineness that, using a mechanical manipulator of his design, it has been possible to inject foreign substances into the protoplasm of living cells. His demonstration in Philadelphia (1921) excited me to the belief that instruments of this type might become valuable as aids in the solution of a number of problems which concern the behavior of the renal vessels. Dr. Wearn, learning of this thought, transmuted it into the suggestion that by means of such a pipette it might be possible to enter the capsule of Bowman and withdraw the fluid as it collected there, with the hope of subjecting it to study.[15] Our joint efforts resulted in the construction of a simple apparatus by means of which a slender pointed tube could be introduced into the intracapsular space and the glomerular fluid collected. Refinements of current methods of testing were introduced so that the minute quantities of fluid available could be subjected to accurate qualitative tests. The filtration theory of Ludwig states that as a result of pressure in the intraglomerular capillaries a protein-free filtrate from plasma passes through the walls of the glomerular capillaries into the space within Bowman's capsule. Our first task, after sufficient manipulative skill had been cultivated, was to test the fluid so obtained for protein. In some fifteen experiments the acetic acid-potassium ferrocyanid test was applied with negative results. Similarly tested a 1 to 100 dilution of frog's plasma gave unmistakable reaction. In other experiments the glomerular fluid was examined for chlorids and in still others for sugar. The urine of the frog kept in fresh running water contains only a faint trace of chlorid (as a rule not more than 0.05 per cent), and if the frog is kept for a day or two in distilled water the urine became completely chlorid-free as judged by the usual

test. The glomerular fluid taken from Bowman's capsule of such a frog contains chlorid in impressive quantity.

The bladder urine of frogs, kept under ordinary conditions, contains no sugar detectable by Fehling's solution. The glomerular fluid, however, always reduces Fehling's solution when drawn from frogs whose blood contains detectable amounts of sugar. In our first experiments, made during the months of November and December, no reducing power could be detected in glomerular fluid, but when the blood of these frogs was examined by McLean's method sugar was found to be absent. On repeating the experiment during these months with frogs which had been injected subcutaneously with small amounts of glucose unmistakable reduction tests were obtained in the glomerular fluid. If sugar was injected in sufficient quantity to establish a blood-sugar concentration of 0.066 per cent or more, then sugar appeared in the bladder urine, but in such instances the degree of reduction by the glomerular fluid was decidedly greater than that by the bladder urine.

These experiments, then, revealed by direct tests the absence of protein and the presence of chlorid and of sugar in the fluid leaving the blood stream flowing through the glomerular capillaries, and are completely in accord, in so far as they go, with the demands of the filtration theory. They contain incontestable proof of the reality of reabsorption within the tubules, and provide the basis for further argumentative support of the view that the glomerular function is a physical rather than a "vital" or "secretory" one. Frogs, as we keep them in our tanks, get little or nothing to eat, and living in fresh water their supply of salts is extremely restricted. If they are to survive, they must retain their bodily store of salt and their nutrition is certainly largely dependent upon conservation of the carbohydrates in their tissues. The experiments show that the glomerular process is one which is not adapted to these conservations and that the escape of chlorid and of sugar which takes place there in these animals, disastrous if uncorrected, is actually corrected by the activity of the epithelium lining the tubules. Such lack of adaptation to the needs of the organism is not commonly encountered in the case of processes which we designate as vital or secretory and may be regarded as indirect evidence that the glomerular process is a physical one.

Another aspect of this matter, however, has become evident as the result of a further series of experiments designed to secure

information of the quantitative composition of glomerular fluid in comparison with blood plasma and bladder urine. At first it seemed hopeless to attempt to subject amounts of fluid ranging from 1 to 5 mg. in weight to the various manipulations which are involved in any quantitative procedure. The question, however, is so fundamentally important, from the standpoint of our conception of renal function, that it warranted extraordinary effort. Prof. Theodore Richards, of Cambridge, in his study of the atomic weights of sodium and chlorin, introduced the nephelometric method of estimating silver chlorid in extremely small amounts.[16] We spent months in practice with his method as applied to minute amounts of known NaCl solutions, and at the end of a distressing period of probation were consistently able to estimate amounts of NaCl of the order of 0.01 mg. contained in 0.002 cc. of water, with a degree of accuracy not far removed from that which obtains in ordinary quantitative work. The average error in the last six consecutive control estimations was 2.3 per cent.

We applied this method to the fluid taken from Bowman's capsule of frogs.[17] In 3 experiments the figures for glomerular sodium chlorid were so nearly identical with those for plasma sodium chlorid from the same frogs (3 to 9 per cent higher), that one could well believe that the demands of the filtration theory as currently accepted were satisfied within experimental error. But in 7 experiments the discrepancy was too great to be accounted for by experimental error. In 5 of these glomerular Cl was higher than plasma Cl by 17 to 31 per cent of the latter; in 2 by 49 and 100 per cent respectively.

In another series of experiments a partially successful attempt was made to estimate urea in glomerular urine. The results are not so numerous and we do not regard them as so accurate as those of Cl. They indicated a decidedly greater concentration of urea in glomerular urine than in plasma.

We see an intimation in these results that the current conception of filtration as derived from filter paper or other inanimate material may require modification when it is transferred to the process of filtration as it may be going on through the walls of microscopic tubes consisting of living capillary endothelium covered by a tenuous layer of epithelium. It may be suggested that these figures indicate glomerular "secretion." I do not think that this is the case. They rather show the necessity of a further scrupulous

investigation of the fashion in which a physical process may be modified when it takes place through the living walls of tubes of capillary size.

The information which has already been presented may be summarized as follows:

Direct evidence has been described showing that fluid issues from the blood during its passage through the glomerular capillaries. Under favorable conditions the rate of issue may be disproportionately large in comparison with the rate of elimination of urine from the whole kidney. These facts correspond completely with Bowman's assumption and with the theory of Ludwig and disprove the recent contentions of Woodland.

Such fluid, collected under the most favorable experimental conditions, contains no protein—a fact which is directly opposed to the recent hypothesis of De Haan,[18] whose work led him to conclude that colloids must normally be eliminated in the glomerulus and reabsorbed in the tubule. It contains both sugar and chlorid, while urine simultaneously collected from the whole kidney contains none. This shows a lack of adaptation of the glomerular process which requires correction, and this is accomplished by reabsorption of these substances during passage of the glomerular fluid through the tubules. This lack of adaptation is regarded as indirect evidence in support of the hypothesis that the glomerular function is physical rather than "secretory," filtration rather than secretion.

Under special conditions of experimentation it has been proved that urine elimination increases or decreases with increase or decrease in pressure in the renal bloodvessels, all other conditions so far as known remaining constant. On the assumption, warranted by anatomic considerations, that the effective site of action of pressure is the glomerulus, this fact affords strong support for the filtration theory.

Quantitative estimation of the chlorid content of the glomerular fluid in some instances is in harmony with the filtration theory; but exceptions to this statement have been encountered which indicate the necessity for a study of the fashion in which capillary forces and vitality of the glomerular membranes may influence the filtration process.

In a discussion of the mode of regulation of glomerular function it is vital to keep in mind the fact that the tuft of glomerular capillaries is interpolated between two vessels having the characteristics

of arterioles. The afferent vessel is commonly described as having a diameter greater by one-half than that of the efferent vessel. Both are supplied with nerves which terminate upon the muscle cells contained in the wall. Whether nerves penetrate the capsule and make connection with the glomerular capillaries may be regarded as uncertain, though a statement to this effect is contained in the writings of the anatomist Smirnow.[19]

In the experiment which I have previously described in which the rabbit's kidney was perfused with blood at a constant rate and in which increase of pressure was found to be associated with increase in urinary output, the opportunity presented itself for a closer examination of the vascular reactions involved.[20] The experiment was repeated with the rabbit kidney, excised from the body and placed in an apparatus (oncometer) designed for recording changes in its size. After perfusion had begun, small amounts of adrenalin were added to the blood, entering the renal artery. Constriction of bloodvessels occurred, as was shown by prompt and decisive rise in perfusion pressure; but at the same time the size of the kidney increased. The conditions of the experiment were such that this increase could have been due only to dilatation of vessels within the kidney. Thus we were confronted with the paradoxical coincidence of vascular constriction and vascular dilatation in the same organ. Similar experiments were made with other organs of the body—legs and intestine—and in these the increase in pressure caused by adrenalin was invariably associated with diminution in size of the organ perfused. If now it is recalled that the renal circulation differs from that in other structures in that the distensible glomerular tufts are inserted between two contractile vessels, an explanation of this paradox suggests itself. The conditions of the experiments were such that constriction of the afferent vessel could have little or no effect upon the volume of blood entering the vessels of the glomeruli; but constriction of the efferent vessels would inevitably cause increase in pressure in the capillaries proximal to it, despite the fact that no decrease in total amount of blood flowing through the kidney could have occurred. Here for the first time, in so far as my knowledge goes, was encountered experimental evidence of the contractility of vessels on the distal side of the glomerular tuft and the suggestion was obvious that we were dealing with a mechanism which is normally concerned in the regulation of intraglomerular pressure, and therefore of glomerular function.

The suggestion had been specifically made by others[21] that glomerular pressure may be subject to regulation by the relative diameters of the afferent and efferent vessels, but up to this time the question had not become accessible to experimental approach.

In order to relieve our experiments of the stigma which is commonly attached to perfusion experiments in which reduction of variables is secured at the expense of normality of conditions, we planned a series of experiments based upon this thought: The efferent vessel is by common consent smaller than the afferent vessel; an equal degree of vasoconstriction involving the two vessels alike could be expected to produce a greater increase in frictional resistance in the smaller vessel than in the greater. Hence if one could select a dosage of a substance whose action included constriction of renal arterioles of exactly the suitable degree of magnitude, he might expect to demonstrate a greater degree of obstruction in the efferent vessel than in the afferent, and the expected manifestations of such action would be a coincidence of slight increase in general aortic pressure, diminution in volume of blood flowing through the kidney, increase in size of the kidney and increase in urinary output. After many trials a few experiments have been successfully carried through in which we think the technical demands of the problem were successfully met, and the results completely correspond with the hypothesis on which the experiment was based.[22] In eviscerated rabbits minute dosage with adrenalin, with pituitary extract and with barium chlorid, gave rise to the coincident events upon which I have laid emphasis.

While we were unable to imagine another explanation equally acceptable, an intense desire was aroused for finding another method of test of the hypothesis. It was this desire which led me to think that it might be possible to subject the frog's kidney to methods which permit direct microscopic observation. If such method should prove successful we might obtain direct visual evidence that constrictor substances acting in high dilution produce a greater degree of constriction of the efferent than of the afferent vessel. I invited Dr. Schmidt to collaborate with me in the effort to apply the methods which were at that time being developed by Professor Krogh in other connections, and we soon discovered that it was a relatively simple matter to subject the glomerular circulation of the frog to direct inspection.[23] So far as I know, this had not been previously successfully accomplished. Our first experiments were

designed to discover whether the intravenous injection of minute amounts of adrenalin were capable of causing an enlargement of the glomerular tuft in a manner compatible with the conditions which I have presented. The results in the main were favorable to our conception. In many experiments the introduction of 0.001 mg. of adrenalin caused flow of blood through the glomerular channels to be retarded, and caused measurable increase in the diameter of the capillary tuft. This was regarded as evidence that the efferent vessel contracted. We could not subject the efferent and the afferent vessels to direct measurement, because as a rule their outlines were obscured by overlying tissue.

While this result was in harmony with those of the mammalian experiments, we conceived one source of possible error as attached to it. Adrenalin not only affects the vessels of the frog's kidney but also those of other tissues; it also increases the activity of the heart. The effect, therefore, which we observed might conceivably be the result of increased blood supply to the kidney consequent upon cardiac stimulation and increased aortic pressure. It was therefore incumbent to design a perfusion experiment with the frog's kidney similar to that which had been made with the rabbit, so that the bloodflow through the frog's kidney should be constant regardless of the state of dilatation or constriction of the renal vessels. That there are technical difficulties to be encountered in such an experiment is obvious and a successful attempt to overcome this has only recently been made in collaboration with Mr. Bradley and Dr. Barnwell: Two syringes of identical caliber were filled with the whole blood from other frogs and arranged so that the contents of either could be driven at constant rate through the vessels of the kidney *via* the renal arteries. Adrenalin to make a concentration of 1 to 500,000 was added to the blood in one syringe. The animal was adjusted on the stage of a microscope provided with a photomicrographic camera so that photographs of glomerular tufts could be taken at frequent intervals during the course of the experiment. Substitution of blood containing this minute amount of added adrenalin for blood containing none caused an unmistakable increase in the size of the glomerular tufts which were under observation. Simultaneous records of pressure in the renal artery and of the amount of blood issuing from the renal vein showed the characteristic constriction of renal vessels but without any diminution in the rate of passage of blood through the entire

organ. The objections which had been made to the acceptance of our conclusions from the experiment on the intact frog seem, therefore, to have been overcome, and we regard this as strong evidence that an increase in intraglomerular pressure may result from constriction of the efferent vessel.

In these experiments attention has been concentrated upon effects which may be produced by minute amounts of the substance adrenalin. We were not primarily interested in the action of this substance as a drug; its great interest for us lies in the fact that it is a hormone which normally circulates in the blood and takes part, we believe, in circulatory adjustments of the most exquisite kind. Its action on bloodvessels, as is well known, is identical with that of sympathetic nerve stimulation, and hence in exposing the intricacies of its action we gain information which is applicable also to nervous control of the renal vessels.

These experiments provide the basis for thinking that very small amounts of adrenalin or very slight stimulation of sympathetic nerves to the kidney may increase intraglomerular pressure by more effective action on efferent than on afferent vessels; while larger amounts of adrenalin or more intense nerve stimulation, by causing constriction of both, lessen both glomerular pressure and glomerular bloodflow. The former influence would result in diuresis; the latter in diminished urine; and it is known that each of these effects may be elicited by adrenalin if dosage be suitably chosen. It seems to me wholly probable that both types of action may be exerted by concentrations of adrenalin which exist at different times in the arterial blood as the result of activity of the suprarenal glands.

Another aspect of the same problem concerns the action of dilator substances. It has long been known that substances which pass readily into the urine and which cause diuresis cause also dilatation of the renal bloodvessels. I refer to increased water content of the blood, to such salts as sodium chlorid, sodium sulphate, sodium bicarbonate, and to sugar, to urea, to caffein and its derivatives. It is at once obvious that any substance which dilates renal bloodvessels without simultaneously producing a fall in aortic pressure will thereby increase the rate of bloodflow through the kidney. Such increased bloodflow *per se* would be a diuretic factor, for the reason that the rate of renewal of contact of fluid from which filtrate is produced with the membranes through which

the filtrate passes would be increased. But whether or not intraglomerular pressure will be increased by vascular dilatation of the kidney will depend upon the relative degree of action upon afferent vessels and upon efferent vessels or vessels distal to the glomerular tuft. The question is therefore pertinent whether such substances as I have mentioned possess the power of dilating the afferent vessels to a greater degree than the efferent vessels.

There were some *a priori* reasons for imagining that this might be the case. We have proved that between the afferent and the efferent arteriole the blood plasma is concentrated by loss of fluid which contains no protein. Consequently the colloid content of the plasma of the blood which is flowing through the efferent vessel is greater than that of the plasma of blood flowing through the afferent vessel; the question therefore arose whether the colloid concentration of fluid in which a vasodilator substance is dissolved may affect the intensity of its action. This suggestion, made four years ago,[24] has only recently been subjected to experimental test. Hamburger's modification of Ringer's solution was adopted as a suitable fluid with which to perfuse the vessels of the frog's kidney from a glass reservoir in the usual way. Four solutions were prepared for a single experiment, two containing as a colloid purified acacia in concentration of 3 per cent. Two other solutions were similarly prepared in which the colloid concentration was 6 per cent. Caffein in amount to make 0.1 per cent was added to one sample of the 3 per cent acacia, and to one sample of the 6 per cent acacia. The arrangement of perfusion reservoirs was such as to permit accurate comparison of the dilating action of 0.1 per cent caffein in 3 per cent acacia with that of 0.1 per cent caffein in 6 per cent acacia. Results were expressed in terms of rate of flow through the organ per minute, perfusion pressure being maintained constant. The result exceeded expectations. In every instance it was found that the dilator action of caffein in 6 per cent acacia is very markedly less than in 3 per cent acacia. Similar results were obtained in experiments in which sodium nitrite and sodium chlorid were tested.

These results show that the peculiar arrangement of the glomerular capillaries in relation to the afferent and efferent arterioles is such that substances which dilate these arterioles produce greater dilatation of the afferent than of the efferent. Thus intraglomerular pressure is raised and increased filtration occurs. Since we

know that renal vessels react very sensitively to dilator substances, we can see how it is that a slight increase in water, salt, urea content, etc., of the blood automatically produces such an alteration of these vessels as to provide conditions favorable for increased glomerular elimination and hence for ridding the blood of such excess.

While our first observations on the effect of minute doses of adrenalin on the size of the glomerular tuft were in progress, other features of the glomerular circulation became apparent, and it was soon evident that these might properly be looked upon as evidences of the fashion in which glomerular function is adjusted to bodily requirements.[25] Some preparations of the frog's kidney were encountered in which very few glomeruli were visible; in others many were to be seen. The visibility of the glomeruli was dependent upon the presence of blood corpuscles within their capillaries. We soon found that the number of visible glomeruli in a preparation in which it was small could be increased by many of the common means of increasing renal circulation, such as section of the sympathetic nerve supply, injection of salt solution, transfusion of blood, injection of salts, of sugar, of urea, etc. On the other hand, the number could be diminished by means which are known to produce constriction of renal vessels, such as stimulation of sympathetic, large doses of adrenalin, or of pituitary extract. These observations yielded proof that in the frog's kidney the fraction of the total glomerular equipment which receives blood and hence which functions at any one time is variable, and thus evidence is afforded in support of the conception that the degree of glomerular activity of the whole kidney is susceptible of adjustment by increase or decrease in the number of glomerular units which are active. This conception was very clearly stated sixty-five years ago by Hermann,[26] a colleague of Ludwig's, but, so far as I know, no definite experimental evidence in support of it has previously been advanced. It is well known that comparatively slight changes in the composition of the blood—changes which are hardly discoverable by chemical means—are capable of producing a diuretic response which seems disproportionately great. If we conceive that a renal vasodilator substance increases the rapidity of renewal of blood plasma in contact with glomerular surface, increases intraglomerular pressure by a greater degree of dilating action upon the afferent than upon the efferent vessel, and in addition causes an

actual increase in the number of glomerular units involved, we have the basis of an explanation of such apparent disproportionate effects. It will be recalled that the work of Gotch, Keith Lucas, Lodholz, and Adrian[27] showed that the intensity of response by muscle to stimulation of its motor nerve is dependent upon the number of fibers in the nerve which take part in the transmission of the impulse. It will be recalled that Krogh showed that the number of patent capillaries in a muscle varies with the physiologic state of the muscle.[28] Our observations show that the number of glomerular units which take part in renal activity may similarly vary to meet changing demand on the part of the organism for excretory function.

These observations on the frog's kidney will not be accepted as immediately transferable to the physiology of the mammalian or human kidney without question. Thus far it has not been possible successfully to subject the mammalian kidney to methods of direct observation. But in respect of variability of number of glomeruli involved in the function of the whole kidney at any one moment, indirect methods are available. Kanolkhar,[29] in London, injected hemoglobin solutions intravenously into animals, removed the kidney and in thick sections of the cortex counted the number of glomeruli which showed traces of hemoglobin and of those which did not. He came to the conclusion that events similar to those which we had described in the frog's kidney took place in the mammalian kidney. Dr. Hayman and Dr. Starr,[30] in our laboratory, have carried through a series of experiments similar to these in design. They used Nelson's method for estimating the number of glomeruli.[31] This consists in staining the glomerular tufts by passing a solution of Janus Green B through the renal vessels, dissecting the cortex away from the medulla, and counting the stained tufts in a small weighed section of the cortex. Knowing the weight of the whole cortex, the total glomerular count for the whole kidney is easily ascertainable. After convincing themselves of the reliability of the method, they found that the number of glomeruli in the two kidneys in a normal rabbit is approximately the same. Then the following procedure was adopted. From the anesthetized rabbit suitably prepared, one kidney was excised without hemorrhage, and laid aside for subsequent enumeration of the total number of glomeruli in it. The condition to be studied was then established in the animal, (that is, injection of diuretic, of

adrenalin, and so forth) a solution of Janus Green B injected into the aorta above the remaining kidney, and within twenty seconds of the end of the injection this kidney was excised. Obviously the dye could reach only such glomeruli as were receiving blood at the time of injection and during succeeding seconds. Glomerular count of the intravitally stained kidney compared with the total glomerular count of the other showed the fraction of glomeruli which were receiving blood during the presence of the dye in the circulation. A long series of experiments was made, the results of which are convincing. They showed that from 50 to 85 per cent of the total glomerular equipment of the rabbit receive blood under control conditions. If a diuretic, such as caffein or NaCl, was given from 95 to 100 per cent of glomeruli receive blood. If graded doses of adrenalin were given, or if vasoconstriction were produced by inhalation of $CO_2$, or if the splanchnic nerve were stimulated, the number of glomeruli receiving blood could be diminished at will to 40, 30, 20, 10 or 5 per cent of the total glomeruli present. These experiments appear to me to furnish adequate proof that the observations made on the frog are acceptable for the interpretation of events which take place in the mammalian organ.

Proceeding from the conception that mechanisms are at the disposal of the kidney, whereby a greater or smaller number of its glomerular units may be utilized in the filtration of fluid from the blood in accordance with the excretory requirements of the body, we may properly ask how it is that damage is avoided to those glomerular structures through which temporarily no blood is flowing? One of the oldest observations in the history of renal physiology is to the effect that interruption of the renal circulation for a short time (minutes) results in albuminuria when the interruption has ceased. If, then, during any prolonged period the kidney uses, let us say, only 60 per cent of its glomeruli, how is it that the other 40 per cent escapes the damage which could be expected to result from lack of circulation through them? The answer to this question begins in observations which were made immediately after we had discovered how to look at the glomerular circulation in the frog's kidney. It was seen that the flow of blood through the glomerular capillaries in many experiments was not continuous, but was irregularly intermittent. This intermittence was not synchronous with the heart beats, nor was it uniform or regular for individual glomeruli which could be simultaneously

observed. This observation suggested the probability that while the total number of glomeruli of the kidney were not necessarily suffused with blood at any one moment, yet by individual variations of bloodflow in individual glomeruli the total glomerular equipment might be suffused within a period short enough to prevent the damage which more prolonged anemia would entail; and this suggestion was adopted as an interpretation of the broader significance of the observed interruptions in glomerular flow.

But how this phenomenon of intermittence is produced was for a long time a complete mystery. It became clear that the intermittent cessations of bloodflow through individual glomerular tufts were not due to constrictions of capillaries composing the tufts. It could be seen that intermittent flow included the arterioles leading to the tuft, and hence the glomerular cessations are in reality arterial or arteriolar phenomena. Finally Langley's work[32] on the nervous control of the smaller arteries in the web of the frog's foot was encountered, and its bearing upon our problem recognized. He showed that when a nerve supplying a vascular area in the frog's web is stimulated repeatedly the resultant constrictions of the smaller arteries do not uniformly involve the same vessels; vessels which contract to one stimulus are not necessarily the same as those which responded to the preceding one. He made the suggestion that the physiologic condition of the muscle of the arteriole may so vary as a result of its contraction that at one time it may be refractory to a stimulus to which it responds at another. This led me to think that in the kidney the smallest arterioles might undergo alterations in their readiness to respond to constrictor influences and that such alterations might be responsible for the observed intermittence. In harmony with this thought was the observation that intermittence is most apt to be encountered in the frog if the upper part of the spinal cord has not been injured in the process of destroying the brain, the operation which we use to avoid the necessity of anesthesia. The upper part of the spinal cord in frogs contains a large share of the central nervous mechanism for controlling the caliber of the bloodvessels. It appeared, then, that it might be possible to produce artificially an intermittence of the glomerular circulation by subjecting the vessels of the kidney to a constant constrictor influence of a moderate grade of intensity. Three groups of experiments were made. In one the central end of the sciatic nerve was stimulated during observation of bloodflow

through a group of glomeruli; in another the ramus communicans from the fifth spinal nerve which contains vasoconstrictor fibers to the kidney was stimulated; and in the third a dilute solution of adrenalin was injected at an extremely slow but constant rate into the abdominal vein. In each experiment a group of glomeruli was closely watched before, during and after the period of stimulation. It became very clear that each of these three means was capable of inaugurating in a previously uniform glomerular circulation an intermittence precisely similar to that which we had previously seen occur spontaneously. And hence we have the basis for belief that when the bloodvessels of the kidney are subjected to a constant nervous or chemical constrictor stimulus the response exhibited by the vessels concerned is an intermittent one. We picture the process to occur as follows: It has been known since the time of Lister and Cohnhein that if a vascular area is rendered anemic by clamping its artery for a time, when blood is readmitted, the vessels are dilated as though their tonus had been diminished by the asphyxia to which they had been subjected. Some years ago I found that when the vessels of the heart or the vessels of the leg of a dog were perfused with fully oxygenated Ringer's solution the substitution of identical Ringer's solution containing no oxygen caused them to dilate immediately.[33] We may therefore regard it as proved that lack of oxygen has a dilator influence upon arterial muscle. If, then, a small artery in the kidney is constricted as a result of a nervous or chemical influence so that no blood passes through it, the asphyxia of its muscle so induced leads to a progressive decrease in its power to continue reacting to that stimulus; so that eventually, assuming the stimulus to be moderate in degree, the muscle must relax, the artery opens and bloodflow through it is resumed. When bloodflow returns, and with it adequate nutrition of the muscle wall of the arteriole, this again becomes responsive to the constrictor stimulus and again the vessel may close. We may conceive such a process, involving many vessels, and hence many glomeruli, as capable of producing just such an intermittence as I have attempted to describe.

There is another fashion in which the surface of glomerular capillaries available for filtration is variable. The capillary pathway in the single tuft in the frog's kidney very often can be seen to consist of three primary branchings from the afferent vessel, each of which in turn undergoes a secondary branching. One

frequently sees that the blood current entering a glomerulus flows largely into one of the three primary divisions and scantily into the other two. In some instances only one capillary channel will be seen in a tuft, but if any one of the various vasodilator influences which I have mentioned are introduced into the blood stream other capillary channels in this tuft may open and become visible by reason of the stream of corpuscles passing through. I have spoken of intermittence of the glomerular circulation, using this term to indicate the fact that blood often ceases to flow temporarily throughout the whole tuft; intermittences of individual capillaries within a single tuft have been plainly seen. In the most striking illustration of this fact which I have encountered the blood current through a tuft during the early minutes of observation was confined to one apparently dilated capillary. While I was watching the flow of blood through this a second capillary suddenly made its appearance, branching from the origin of the first; presently a third similarly appeared, and during the succeeding minutes of observation these two alternately opened and closed, while bloodflow through the first remained steady and uninterrupted. When viewed by reflected light under varying circulatory conditions, remembering that the capillary pathway is discernible almost only by corpuscles passing through, the appearance of a single tuft may be so different at different times as to make it difficult to believe that it is a single structure which is under observation.

For a long time we were under the impression that these changes in capillaries within a single tuft were caused by changes in the caliber of the capillary presumably brought about as a result of nervous influence exerted upon it. One citation from the anatomic literature can be advanced (Smirnow) indicating that nerve fibrils pass into the capsule of Bowman and are related to the capillaries enclosed within it; but when the changes which occur in the circulation within a single capillary of a glomerulus are more closely observed, using higher powers of the microscope, one fails to discover signs that the caliber of the capillary tube decreased during such interruptions as I have described. Into such a capillary a single corpuscle may be seen to enter. It passes slowly through and disappears, but during its passage it is not distorted as would necessarily be the case were the capillary narrowed, but on the contrary can be seen to rotate on its various axes and apparently to bump from side to side as though floating in transparent fluid

flowing through a relatively wide tube. Observations of this sort have led to the view that alterations in the caliber of glomerular capillaries resulting from their own contractility are yet to be proved. Such events as those just described can be more satisfactorily accounted for by alterations in diameter of the openings from the afferent vessel into glomerular capillaries. We have suggested that these openings may have sphincter-like properties, may undergo rhythmic alterations in tonus and may be more sensitive to constrictor or dilator influence, nervous or otherwise, than is the capillary wall. Indeed, Dr. Schmidt made observations, and I have confirmed them[34] which indicate that constrictions under the influence of adrenalin occur more effectively at branchings of the smaller arterioles in muscle than at intermediate points, and in the older literature are to be found descriptions of phenomena which accord well with this statement. In the very recent work of Landis on pressure within capillaries further evidence has been encountered which is in harmony with this statement.

Another mode of adjustment of glomerular filtration may be mentioned. It is obvious that the glomerular capillaries are in a peculiar situation in that they are enclosed by Bowman's capsule which forms a strong and highly elastic envelope. We know that fluid issues from these capillaries into the intracapsular space from which it flows into the tubule. We know that fluid in different capsules is subject to different degrees of pressure which depend upon the pressure within the glomerular capillaries, upon ease of passage of fluid through the walls of these, and upon ease of exit of fluid down the tubule. Evidence of such varying intracapsular pressures can be obtained by simple inspection of a kidney which is forming urine. The degree of distention of different capsules which come within the range of one's vision is highly different, and if uniform pressure is exerted upon the surface of a kidney by means of a fragment of coverslip, it is seen that the flow of blood may stop completely in the capillaries of one tuft, while it is vigorously maintained in those of another. Regarding the glomerular process as one of filtration, it is obvious that filtration pressure is the difference between the pressure inside the capillaries and the pressure outside. The more rapid the accumulation of the outside pressure, and the higher the point which it attains, the more rapidly must an impediment to filtration accumulate. Such an accumulating impediment must act as an automatic brake to the process.

If one perfuses the frog's kidney with oxygenated salt solution to which a trace of India ink has been added to render the capillary tufts more easily visible, and if the pressure under which the perfusion fluid is flowing through the kidney is suddenly raised, many visible tufts undergo obvious increase in size. Some do not, but if after previous laceration of a few of the capsules of the visible glomeruli a similar increase in pressure is induced, then it is found that the increase in size of the capillary tuft in these is decidedly greater than before. In other words, the capsule of Bowman, which serves as a chamber for collecting the glomerular filtrate and transmitting it to the tubule, is also a protection to the glomerular capillaries enclosed in it, and prevents damage to these capillaries which might result from excessive capilary pressure; by the tension which it is capable of exerting over the fluid which is in it, it can slow down the filtration process. We are as yet ignorant of the pressure which exist in the glomerular capillaries and within the capsular space. The subject is one upon which Dr. Hayman is at present engaged, and the prospect is that we shall shortly have quantitative data by which to measure the correctness of these statements.

In review of the information which I have been able to present which bears on the question of glomerular regulation, it may be said that evidence now exists upon which to base belief that glomerular pressure and hence glomerular filtration is regulated not only by the gross circulatory events which have long been recognized, such as alterations in the arterial pressure, in the venous pressure and in the gross change of the renal vessels in relation to these, but also by fine adjustments of the caliber of the afferent and of the efferent vessel in relation to each other. The mode of adjustment is such as automatically to provide conditions suited to rid the blood of excess of any substances which dilate the renal arterioles and which pass through the glomerular membranes. The more important normal urinary constituents very certainly possess these properties. Evidence has been presented in support of the belief that the action of adrenalin includes constriction of the efferent vessel as well as of the afferent. The proved identity of the vascular actions of adrenalin with the effects of sympathetic nerve stimulation permits the results obtained with adrenalin to be applied to problems of nervous control of these vessels. The suggestion may be made that the normal state of tone of these minute arterioles,

sustained by the tonic action of the sympathetic nerves and of circulating adrenalin is such as to maintain intraglomerular pressure by slightly greater constriction of efferent vessel than of afferent, whereas an increased degree of vasoconstriction must diminish intraglomerular pressure by closing of the afferent vessel.

Glomerular regulation is also secured by changes in the number of glomerular tufts and of capillaries in the same tuft through which blood flows at any one time. This is equivalent to saying that the extent of endothelial surface available for filtration is variable, being increased by influences which dilate vessels and decreased by influences which constrict. Damage to the kidney by prolonged anemia of any of its parts is avoided by the provision of intermittence and this in turn is, we think, dependent upon the action of constrictor influences and the antagonistic dilator action of anemia which results from these.

Extracapillary intracapsular pressure which develops because of the elasticity of the capsule of Bowman, may act as an automatic brake upon the filtration process and at the same time is capable of protecting glomerular capillaries against undue distention from excessive intracapillary pressure.

We have described the process of filtration in the glomerulus as one not adapted to the interests of the organism as a whole, because it indiscriminately eliminates from the blood substances which the body should retain as well as those of which it should be rid. The tubule supplies the correction to this lack. But in the arrangements which have been developed for the circulatory control of the glomerular process we must see evidence of a very high degree of adaptation to the bodily welfare.

I have not touched upon the problem of permeability of glomerular membranes. I am convinced that variations in it occur and will eventually be demonstrated; but the direct experiment which compels belief has not been made.

Before closing, I wish to mention very briefly a series of experiments which may serve to relate some of the observations I have been describing to the practical problem of albuminuria. Four years ago it was suggested that if the period of intermittence of glomerular bloodflow should be slightly lengthened an albuminurina might be anticipated to result.[35] The anticipation was based on the knowledge that temporary closure of the renal artery is followed by albuminuria and upon the evidence provided by

Nussbaum that this is glomerular in origin.[36] Experiments were designed to test this thought and Dr. Starr has carried them out.[37] Normal healthy rabbits, given an intravenous injection of adrenalin in such amount and fashion that its action is maintained for several minutes, subsequently show transient albuminuria. Healthy cats, subjected to insults which they resent and which excite them to fear or rage, subsequently eliminate albumin. When the question was studied in anesthetized dogs under controllable conditions it was found that the course and degree of albuminuria which could be produced by vasoconstrictor influences, such as adrenalin, stimulation of the splanchnic nerve, inhalation of $CO_2$ and so forth, was strictly analogous to that which could be produced by temporary partial obstruction of the renal artery. In exceptional experiments no renal vasoconstriction was produced by these means, and in these albuminuria did not occur; thus showing that the albuminuria was dependent upon the vasoconstriction and was not the result of direct action of the agents tried upon the glomerular membranes. Histological study showed no abnormalities of structure in these kidneys. Similar results have been obtained in man in a study by Dr. Grier Miller, now in progress in the University Hospital, of the effects of ephedrin—a drug of Chinese origin recently studied by Dr. Schmidt and K. K. Chen, in Peking, samples of which have been supplied to us by Dr. Chen. Their work showed that ephedrin causes vasoconstriction similar to but more lasting than that of adrenalin. In the cases studied by Dr. Miller tests made by Dr. Starr for albumin in the urine were positive in those cases in which distinct rise in blood-pressure occurred; negative in those in which it did not. Maximum albumin elimination did not coincide with maximum height of blood-pressure, but followed it.

These results show how renal vasoconstriction can lead to albuminuria and how a diuretic which opens up glomerular vessels which have previously been closed may appear to be a damaging agent upon renal structures, whereas in reality the damage of which the eliminated albumin is evidence was the result of the vasoconstriction which the diuretic abolished.

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# APPENDIX

## PROCEEDINGS

OF THE

## SECTION ON OPHTHALMOLOGY

JANUARY, 1925, TO DECEMBER, 1925

### JANUARY 15

#### Sketch of the Life of Sir Isaac Newton

Dr. Burton Chance read a sketch of the life of Sir Isaac Newton, who harbored in his frail body, which at birth seemed too feeble to live out the day yet survived eighty-five years, a spirit of the greatest industry and inventiveness. His discoveries in the optical sciences and his expositions of the properties of light laid the foundation of all later additions. And to him ophthalmology owes an inestimable debt, yet these greatnesses were only a small part of his general knowledge. Notwithstanding the laudation of his admirers, Newton's was not the greatest intellect bestowed on man, and he should not be regarded as an isolated phenomenon but for whom the world would have been in darkness. In all his labors he was only following the spirit of his day, since other men were working along similar lines and many of his problems are still unsolved, so that we can assent to the message contained in the inscription on his tomb in Westminster Abbey and "rejoice that there existed such and so great an ornament of human nature."

Discussion. Dr. S. Lewis Ziegler desired to record his hearty commendation of the fine historical work that Dr. Chance has

presented before the Section. He had been doing similar research work and therefore realized the amount of labor required to assemble the events of the past in a readable form.

### The Bacterial Power of Aqueous of Second Formation. A Possible Explanation of the Beneficial Effect of the Saemisch Section

Drs. E. M. Landis and H. F. Robertson (by invitation) said that, since in Saemisch section the ulcerated surface is bathed by the aqueous, it was suggested that the beneficial effects usually observed after the operation might be due to a replacement of the normal aqueous by aqueous of second formation, on the hypothesis that the newly-formed fluid contained antibodies not present in normal aqueous.

The problem involved the determination on the relative bactericidal powers of normal aqueous and aqueous of second formation, using for the tests staphylococcus albus and bacillus typhosus.

Previous work concerned itself chiefly with animals immunized to foreign erythrocytes, but in all accounts the aqueous of second formation contained greatly increased amounts of antibodies. The work of Vedder gives a slight suggestion of a similar increase in bactericidal power. By a table comparing the number of organisms alive after sixty minutes' exposure to undiluted and diluted aqueous, by average curves and by graphic means, it was shown: (1) Normal aqueous possesses variable bactericidal powers against staphylococcus, which are markedly increased in aqueous of second formation, both undiluted and diluted; (2) normal aqueous diluted 1 to 10 has little bactericidal power against bacillus typhosus; secondary aqueous is markedly bactericidal.

### 1. A Case of Membrana Epipapillaris. 2. A Case of Probable Extensive Remains of Cloquet's Canal

1. Dr. William Zentmayer presented a case of membrana epipapillaris seen in a man who visited the Wills Hospital because of a foreign body in the cornea. In the right eye there was a somewhat quadrate, veillike membrane covering the entire disk and also extending on to the retina to the nasal side. The papillary vessels and excavation could be indistinctly made out. A curious feature

was the narrow hem which extended around three sides of the membrane.

The noncommittal term of membrana epipapillaris has been given to the various types of adventitious tissues seen at times upon the disk and the peripapillary area. They have been attributed to remains of the hyaloid structure and also considered to be the glial cells of the embryonal vitreous. Dimmer speaks of the similarity of the tissue to that of Kuhnt's central supporting meniscus.

2. Dr. Zentmayer also presented a case of "Probable Remains of the Hyaloid Canal" in the right eye of a child. Beginning at the point of emergence of the vessels from the disk and running upward over the disk and on to the retina, about 3 d.d., there was a sausage-shaped, greenish-white, somewhat prominent mass which at this point became constricted and further on terminated in a flaring brush. Running out from the point of constriction there was a cordlike extension into the anterior part of the vitreous. There is a description of a similar condition by Dimmer, which he looked upon also as a remnant of the Cloquet canal.

Discussion. Dr. P. N. K. Schwenk showed a drawing which he made thirty-seven years ago for Dr. Charles A. Oliver, and reported in the *Transactions of the American Ophthalmological Society*, vol. iv, page 580, which showed a clubbed-shaped body attached to nerve head and extended outward to macula, where it was adherent. This undoubtedly was a shrunken remains of a hyaloid artery. The left eye had a nodule, with small fibers extending from it, floating in vitreous.

## A Brief Survey of Adrenalin Chloride, with Especial Reference to its Subconjunctival Injection

Dr. C. Oram Ring gave a brief survey of the use of adrenalin chloride, with especial reference to its subconjunctival injection. After referring to the recent publication of Dr. Harry S. Gradle, of Chicago, on the subconjunctival injection of the 1 to 1000 solution in 16 cases, he quoted from a letter from Dr. A. A. Stevens, professor of applied therapeutics in the University of Pennsylvania, as to the question of local reaction under varying systemic conditions, the risk involved as to the systemic response to the injection subcutaneously up to 6 minims, the value of the Loewi reaction and the comparison of cocaine and epinephrin:

"It is very doubtful whether the subconjunctival injection of 5 or 6 minims of a 1 to 1000 solution of epinephrin would have sufficient effect upon the general arterial tension to prove harmful, even in the presence of cardiovascular disease and hypertension, which are common accompaniments of glaucoma. Subcutaneous and submucous injections of epinephrin, if not under pressure, have comparatively little effect upon arterial tension, because of the local vasoconstriction and the slow absorption of the akaloid.

"The effects of epinephrin and of cocaine on the pupil, ocular vessels and intraocular tension are qualitatively similar, although those of cocaine may be obtained by local application to the conjunctiva. Both drugs stimulate the peripheral sympathetic mechanism, but the vasoconstricting effect of cocaine is less pronounced than that of epinephrin, and therefore its effect upon intraocular tension is less constant."

After referring to the observations of Knapp, of the dilatation of the pupil after the instillation of adrenalin in the eye as a diagnostic sign in glaucoma, Dr. Ring gave the history of 3 male patients in whom the subconjunctival method was employed, in 1 of whom it was used in both eyes. In each of the 4 eyes there was almost immediate diminution of tension, and in each the reduction was followed in about forty-eight hours by a posterior scleral puncture, with moderate vitreous extrusion in each. The preliminary reduction of tension by the injection, it was felt, lessened the gravity of the situation, as in each of the cases there was advanced cardiorenal disease. It is regretted that the necessity of the cases prevented a careful series of observations as to the approximate length of time the injections would have kept the tension down. In the first 3 of the 4 eyes two months have elapsed and they continue to do well.

Discussion. Dr. S. Lewis Ziegler said that the subject of deep orbital injections of adrenalin and novocaine was discussed by Fromaget before the French Ophthalmological Society in 1921–1922. He noted that ten minutes after injection the scleral vessels contracted, the steamy cornea cleared up and the fundus again became visible. The tension dropped from 140 mm. to 60 mm. He proved this in certain cases by injecting adrenalin and novocaine separately. He concluded that the local action of adrenalin on the ciliary vessels, the ciliary nerves and ophthalmic ganglion produced rapid vasoconstriction and ischemia of the choroid. Dr. Ziegler

added his testimony as to the efficacy of this treatment in preparing almost hopeless cases for successful operation. But the tendency to a sudden hypertony must be watched and a posterior sclerotomy performed if the emergency demands it. He has adopted Galezowski's designation of sclerochoriotomy. He prefers to enter his knife and turn it at right angles on withdrawal, thus making a T-incision as suggested by Parinaud. He always makes a double puncture, locating one between the internal and inferior rectus and the other between the external and inferior rectus.

Dr. Ziegler recommended finger-massage, after the method of Dianoux, as a helpful procedure in these cases.

Dr. William Zentmayer said that this procedure is not without danger, as was shown in one of Dr. Gradle's own cases, in which the physiologic effect of the drug was so marked that he incised the conjunctiva and washed out, so far as possible, the unabsorbed solution.

An interesting application of Dr. Knapp's so-called adrenalin test is that of Schoenberg, who applied it to other members of a family in which a case of glaucoma had occurred, for the purpose of determining whether there was a glaucomatous tendency in the other members of the family, As he recalled, some positive results were obtained by him.

Dr. Ring, in closing the discussion, called attention to the fact that in the 1 case of Dr. Gradle's series to which Dr. Zentmayer had referred, 8 minims of the adrenalin solution had been injected subconjunctivally, whereas in his own cases only 4 minims were utilized. He disclaimed any thought that the procedure, even though followed promptly by posterior sclera puncture, could replace the usually recognized classical operations, but felt that in certain grave cases it could be utilized with definite advantage.

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## FEBRUARY 19

### Melanotic Sarcoma of Iris and Ciliary Body

Dr. Frederick Krauss presented a man, aged sixty-two years, in whom the right iris showed a melanotic mass occupying the lower and outer angle of the anterior chamber. The tumor, except for

its color and irregular contour, could be readily taken for a hyphæma. There was a slight coloration of the sclera over the ciliary body at this point. The pupil dilates well in the superior and inner half; the lower, outer part lags under atropine, the iris being pushed forward. Vision, O.D., 10/50; O.S., 16/30. Tension normal. Directly behind the lens, and apparently springing from the ciliary body, was a large, bluish-white, round mass, almost spherical in outline, a few fine vessels passing over the surface, seen when the eye is directed to the temporal side. The rest of the media appears clear, with a gray nerve and moderate vascular changes due to his age. After a second visit to the Episcopal Hospital Clinic the patient wandered to other eye clinics and suffered from hemorrhages in the eye, as he describes it. One week ago he returned to the clinic. He had no marked pain, but felt that his eye was gradually getting worse.

### A Case of Cicatricial Ectropion Showing Operative Results

Dr. William Zentmayer said that the procedure was one modified from that suggested by Imre, and consisted in the exclusion of a diamond-shaped area including the margin of the lid and a portion of the scar. Lateral incisions were made parallel to the border of the lid from either midangle of the diamond almost to the canthi. The marginal suture was inserted to deepen the cul-de-sac. The result was an absolute correction of the ectropion. The patient was a little girl who had fallen against a hook which lacerated the lid.

### A Case of Bilateral Scleritis

Dr. P. De Long presented a case of tubercular scleritis in a colored man, aged thirty-six years. Vision, O.D., 6/9; O.S., 6/15. During convalescence from an attack of pneumonia, in September, 1924, the writer observed three areas of congestion in the eyes. On the right side the area was down and out; on the left side up and in and down and out. No other involvement of sclera. Slight infiltration at the limbus to the temporal side; no evidence of any definite cyclitis. At 11 o'clock in the iris angle there appeared a small, pin-head-sized nodule. Wassermann strongly positive; tuberculin tests negative; physical examination, negative. Reasons for diagnosis of tubercular scleritis: (1) Disease followed a pneumonia with pleurisy; (2) luetic and usual treatment gave no response; (3) clinical picture suggests a tubercular process.

Discussion. Dr. William Zentmayer said that the patient of Dr. De Long appeared to be one of deep scleritis; but, as Fuchs says, one cannot say whether the condition is superficial or a deep scleritis until the infiltrate is absorbed, when the depth can be judged by the resulting thinning of the sclerotic. In spite of the plus Wassermann, he was inclined to believe with Dr. De Long that the etiology is tuberculosis. The race, the sluggish nature and the recent involvement of the cornea are all suggestive.

## Epithelial Erosion of the Orbit

Dr. Burton Chance exhibited a case of Jacob's ulcer involving the orbital tissues of a vigorous man, which had existed for three years without pain or much discomfort. It had invaded the outer third of the lids and extended deep into the orbit. The external muscles were eroded and lately the cornea had become necrotic. The man had no treatment whatsoever. It is intended to apply radium, with the hope of stopping the extension of the process.

Discussion. Dr. Leighton F. Appleman spoke of the remarkably good results which may follow the use of roentgen-rays in cases of epithelioma as exemplified by a case seen in the Polyclinic Hospital under Dr. Holloway's service. This case showed extensive loss of the left maxillary region, leaving a cavity bounded above by the floor of the orbit, below by the roof of the mouth and posteriorly by the pharyngeal wall. This area had been exposed to the Roentgen-rays by Dr. Pfahler, with the result that the whole cavity was covered by healthy mucous membrane and no sign of active erosion was to be seen. This patient eventually left the Hospital in apparently good condition as far as the local condition was concerned.

Discussion. Dr. George E. de Schweinitz discussed briefly the characteristics of so-called rodent or Jacob's ulcer, namely, the relentless but slow advance of the process, years often elapsing before lesions attain any considerable size, and the absence of involvement of the neighboring lymph glands. He referred to a case, reported a long time ago, in which this type of ulceration exhibited an unusual deliberation in its progress, many years, in fact; but ultimately, in spite of the trial of many methods of treatment, including operations, the patient died of exhaustion. This was before the period when radiation ($x$-ray and radium) were available. In another

patient, also revealing extensive destruction of the tissue, radium, although it did not check the slowly spreading ulceration, relieved the intolerable pain, which, however, is by no means always present in these cases. He believed this was the first time in this city in which radium had been used (it was a good many years ago) in a case of this character. The late Dr. John B. Shober had loaned his supply of radium for this purpose. He believed that it would be worth while to try, now that various methods of radiation had so greatly improved, their effect in the present case.

### An Unusual Case of Orbital Abscess in an Infant: Evacuation through a Fistulous Orifice in the Bulbar Conjunctiva

Dr. William Campbell Posey reported a case of orbital abscess in an eight-weeks-old infant which followed a slight scratch upon the lids. The abscess pointed and evacuated through a small fistula in the temporal bulbar conjunctiva on a level with the horizontal axis of the cornea, 3 or 4 mm. from the limbus. Pressure upon the orbit caused the discharge of a large quantity of pus through this orifice. The discharge ceased after some days; a probe was passed through the fistula posteriorly, but no pocket of pus was opened up. Incision into the floor of the orbit was also negative. Radium was applied, on account of the possibility of the existence of a growth; but a few days later, owing to an advance in the inflammation, the discharge of pus reappeared and continued until the abscess drained and the eye resumed its normal position in the orbit. A small ulcer which appeared on the cornea near the fistula rapidly cleared under appropriate treatment. The ophthalmoscope gave no evidence of injury to the optic nerve from the orbital inflammation.

Dr. Posey spoke of the rarity of such cases, but referred to a case of his own where an orbital abscess had pointed in the lower conjunctival cul-de-sac. Other cases in the literature record pointing through the conjunctiva, usually in connection with the insertion of a rectus muscle.

Dr. Posey spoke of the frequency with which orbital abscess is derived from disease of the superior maxillary bone, and referred to a paper read by him before the American Medical Association, in 1912, entitled, "Orbital Cellulitis from Disease of the Superior Maxillary in Children." In this paper the anatomy of this bone

was reviewed and its liability to be infected in infancy, owing to its cancellous structure at that age. The infection of the alveolar border by dirty nipples in nursing was held to be a not infrequent cause of disease of the bone, also antral disease, orbital cellulitis following infectious fevers doubtless preceding from a primary involvement of this cavity.

Discussion. Dr. William Zentmayer said that in involvement of the superior maxillary sinus there sometimes results a cicatricial ectropion of the lower lid, due to a caries of the bone and a resulting sinus. He had seen one such case with Dr. Posey, and in another he had operated by making an incision around the adherent cicatrix, allowing this tissue to remain attached to the bone and then uniting over this the skin. Such a procedure, he had been informed, was unsurgical, as it may lead to a fistula; but it did not occur in his case.

## First Book on Diseases of the Eye

Dr. Burton Chance said that at the recent dinner of the College Dr. Keen, in referring to the objects treasured by us, cited "the first book on diseases of the eye" as one of our most precious possessions. It has occurred to the writer that it might be of interest to know something about one of the milestones of our art, which was laid eighteen years before this continent was discovered, a copy of which now, four hundred and fifty years after it was published, reposes in our Library.

The book is entitled, *Benevenuti Grassi Hierosolomitani Doctoris Celiberrimi ac Expertis Simi de Oculis Eorumque Egritudinibus & Curis Feliciter Incipit.* It was printed in Ferrara in 1472, and therefore is ranked among the first books printed by movable type. It is probable that there are but two other copies in America, one in the Surgeon-General's library, the other in the Morgan library. Because of its great rarity it possesses a sentimental as well as medical historical value. The author is listed in the Surgeon-General's library index as "*Grapheus*, Benevenutis." His name, however, can be found in many forms—Grassus; Bienvenu Raffe; Benevenutis de Jerusalem (as expressed in the title of our book); Binimitus Grafton; Benevenutus; and Ben Vengut de Salern. Under one or other of these names he was known as the most famous oculist of the Latin, European and Christian Middle Ages. The time and place of his birth and his death are unknown; Hirschberg

is inclined to place him in the XIIth Century; but there is greater certainty that he did not flourish before the XIVth; Guy de Chauliac, in 1363, knew of him. He is believed to have been a Jew, of Jerusalem, while it is known that he studied at Salerno and that he practised in Italy and in the south of France. His manuscript treatises, *Practica Oculorum* and *De Morbis Oculorus*, were for centuries the standard works throughout Christian Europe, and copies of these treatises in the early western European languages, as well as in Latin, are still extant. This printed book of 1474 is a revision of the earlier treatises. It contains little of original value, but is rather an epitome of the accepted methods of the practitioners of the author's era, based upon the writings of the Ancients, which were well known to the physicians of western Europe, as well as upon those of the Arabian writers.

The book consists of seventy pages of twenty-five lines each, the type being rather heavy yet beautifully clear and perfectly aligned. There is no title page, as is usual in the early books, and the printer's name is abbreviated below the last lines of the last page. Below the name are two "F's" and four "I's" which are believed to indicate that it was "completely finished" in the year "1474," the printer having used similar signs in other books whose dates have been certified as of years earlier and later, as, for instance, "F——F——II" and "F——F——V," being, respectively, "1472" and "1475."

The intimate history of our volume is not known. The binding is not the original covering. On the margins of several of the pages are notes and corrections written in an antique hand in Latin. So precious is our copy, for it is one of the first edition, that no one is allowed to take it away from the case where it is kept.

## A Muscle Model for the Demonstration of Ocular Motility

Dr. Luther C. Peter demonstrated a model designed by Dr. Edwin B. Miller and himself to aid the student to visualize the normal action of the ocular muscles and to correlate the symptoms when one or more of these muscles become paralyzed. Parts of the model are not unlike the small model of Knapp. It is, however, built on a larger scale, and an attempt has been made to maintain the relative size of the eyeballs and muscle lengths, together with the muscle planes as found in the living subject. In a mechanical

device it is not possible to accurately indicate and execute all ocular movements, but the model illustrates satisfactorily the movements of each muscle from primary to secondary position. Springs of varying strength are attached to the muscles to maintain the eyes in balance or in position of functional rest.

By detaching one of the cords, such as the superior rectus, for example, to simulate a palsy, the eyeball is placed relatively as found in an ocular palsy. The eye is down and out and the vertical meridian of the cornea is rotated outward.

In order to indicate the symptoms as observed in paralysis, a head is attached, which, by means of a ball-and-socket joint, can be placed in its proper position as seen so often as the patient walks into the office.

A second attachment is that of a diagram which shows the following phenomena: (1) In an approximate way, the physiologic action of each individual muscle and the tilting of the corneal meridian by each muscle from "eyes front," or in primary position. To illustrate, the right superior rectus moves the eyeball up and in, and rotates the upper corneal meridian nasalward. (2) The position and leaning to of the false image. In the case of superior rectus palsies it is up and to the nasal side (crossed diplopia), and the leaning of the false image is to the left. (3) The limitation of movement. (4) The direction of shoulder-tipping, when present. (5) In a modified way, the direction of the face in vertical palsies is indicated as though looking in the direction of the maximum vertical pull of the paralyzed muscle in health.

A third attachment records yoke or conjugate muscles of the two eyes, and the direction of their pull from "eyes front," as well as the leaning of the vertical corneal meridians under the action of these muscles. This diagram is a composite of the first one mentioned, in which the chart of one eye is superimposed on the other. On the reverse side of the diagram are recorded the associated right- and left-hand rotations and right- and left-hand elevators and depressors.

The model is intended for teaching and lends itself to demonstration before a large class, as it is of sufficient size to be seen at a considerable distance. We are indebted to the Lenox Instrument Company for the making of the model and in solving the mechanical problems involved in the designing of the model.

Discussion. Dr. Edwin B. Miller said that in devising this model it was found advantageous to arrange the dimensions in exact proportions to the normal eye globes—23 cm. in diameter and the center of rotation exactly 10 cm. from the retina and 13 from the cornea. The muscles are all about the same length in centimeters as the normal muscles in millimeters. The superior and inferior recti are placed at an angle of 223 degrees, while the obliques are at an angle of 39 degrees. The difficulty with the small models was that they were very fragile and could not be handled by a body of students without constantly getting out of order. The exact pupillary centers could not be worked out, because it would make the model too massive, and there is a slight error in the distance between the optic foramina.

## A Variety of Injury to the Lens Detectable only by Slit-lamp Observation

Dr. Basil Graves gave an account of a condition in the eye of a man, now aged forty-three years, who, having practically normal vision, showed on retinoscopic examination a faint cataractous change above and temporalward in one eye. This change, examined in the fine optical section, reveals itself as a thin, plaque-like zone of increased relucency between the adult and outermost embryonic zone-lines, rather nearer to the adult line. Retroillumination, and also the fact that it is visible by retinoscopy, indicate that the change is obstructive to light; it is "cataractous." Among other details the case shows two features of outstanding interest:

1. This pathologic zone is situated rather central to the line of the surface of the adult nucleus, and it is, therefore, justifiable to assume that, if it originated beneath the capsule and migrated centralward with growth of the cortex, its subcapsular origin must have dated from a period which preceded the subcapsular origin of the face of the adult nucleus beneath which it now lies. The adult nuclear zone-line, although it has been seen as early as the ninth or tenth year of life, in all probability usually comes into being beneath the capsule at a rather later period. Conforming to these chronological facts this patient gives the history that at the age of ten he received a blow on this eye with an apple, on account of which he was kep in bed with a bad eye for three weeks.

2. The second feature of interest is that, while a great part of this

pathologic accessory zone is truly obstructive to light, *i. e.*, it shows as an opacity by slitlamp retroillumination and against the red background of the fundus-reflex by retinoscopy, its lowest part is not obstructive to light and does not show by retroillumination in this manner. Hence, as shown by part of this pathologic area, it seemed possible to have a pathologically relucent zonelike feature of traumatic origin which, showing by direct illumination in the optical section, is of insufficient density to show by retroillumination. Following this observation it occurred to the speaker whether it might be possible to find, in the lens of an eye examined some time after it had received concussion injury, a change which, while being sufficient to reveal itself as such by direct illumination in the optical section, nevertheless might fail anywhere to show itself against the fundus-reflex by retinoscopy. The examination of various eyes which had been subject to concusion injury eventually succeeded in finding of this anticipated feature.

A man, aged twenty-one years, came to the writer three and a half years ago, a month after he had received a blow in the eye from a cricket-ball. As the result of this blow he lost central vision, owing to posttraumatic pigmentary degenerative changes at the macula. Retinoscopic and ophthalmoscopic examination now show his lens, and for that matter all his media, to be absolutely clear; but the slitlamp thin optical section shows a pathologic accessory relucency zone situated not far beneath the anterior capsule, its exact situation being a little further behind the normal reduplication (subcapsular) line than this line is behind the anterior capsule. If successive optical sections are taken through various parts of the anterior region of this lens, this accessory zone can be mapped out as having a definite shape and covering a relatively wide area. It should be emphasized that this feature in this case is revealed only by direct illumination in the thin optical section, and is revealed in no manner by other methods, *e. g.*, retroillumination. Hence it is not an opacity in the scientifically accurate sense that the term opacity should be used in opthalmology.

In conclusion, this case shows that concussion injury to the eye can produce, though perhaps rarely, some sort of disturbance of an unknown nature beneath the anterior lens-capsule, so that with subsequent migration by cortical growth of that region which formerly was subcapsular an accessory pathologic relucency zone, visible only by direct illumination in the optical section, may at a later

date be found in the deeper cortex; and both casts show that the depth of the situation of such traumatic changes within the cortex will depend on and increase with the interval that has elapsed since the receipt of the injury. Various drawings were shown illustrating the principles concerned.

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## MARCH 19

### A Case of Congenital Loop of Veins Extending into the Vitreous, Bilateral. A Case of Bilateral Facial Paralysis

Dr. Mary Buchanan (by invitation) exhibited a case of congenital loop of veins extending into the vitreous, in a colored girl, aged fourteen years. The loop projected from the center of the disk, and the anterior tip was seen clearly with +4 D. on the right side and +2 on the left. The eyes were otherwise normal and the vision with a low + cylinder equaled 5/5 in each eye.

Dr. Buchanan also showed a case of bilateral facial paralysis involving brows, lids, cheeks and upper lip, associated with insensitive corneæ. Lower lip and chin were not affected. The muscles were atrophied and third of normal, but the corneæ were covered. The patient, a girl, aged thirteen years, is one of a family of 14 children, 9 of whom are dead; 3 of those living having some form of paralysis. The ophthalmoscope showed the disks well defined and vessels normal. Hearing unimpaired; Wassermann negative; *x*-ray of the chest revealed no pathology; *x*-ray of the head showed inner table of skull atrophied, with the convolutions clearly defined, with the frontal suture spreading. The differential blood count revealed the following: Red cells, 3,999,000; white cells, 6900; hemoglobin, 70 per cent; small lymphocytes, 43 per cent; large lymphocytes, 6 per cent; polymorphonuclear leukocytes, 51 per cent. The vision with correcting lenses = 5/6 in each eye. Dr. Wilson made a neurological examination and believes the case one of muscular dystrophy, familial in type.

### A Case of Ciliary Tuberculoma

Dr. Burton Chance exhibited a case of tubercle of the iris in a young girl, aged eleven years, which had come under his observation late today. The disease had been noticeable only in the past few

weeks; it was painless and had come on without any known cause. There are several masses of various sizes on the iris, the largest covering the inferonasal third, blocking the angle and pressing on the cornea. Besides miliary nodules on the face of the membrane, there are four others of considerable size on the larger circle and one distinct mass on the small. There is distinct punctate keratitis with marked ciliary injection.

## A Case of Proliferative Retinitis

Dr. L. Waller Deichler exhibited a case of proliferative retinitis which he brought before the Section because of the bloodvessel proliferation in the exudates themselves, transforming them into connective-tissue structures.

The patient, a man, aged forty years, reported to Dr. Pontius' service at Wills Eye Hospital, January 26, 1925, and gave a history of imperfect sight for one year. Vision, O.D., 20/30; O.S., 20/40. The lids, lachrymal apparatus, corneæ and anterior chambers were normal. Pupils equal and prompt in reaction. Tension normal. Under homatropine the right eye showed small pinpoint opacities on the posterior surface of lens, otherwise the media were clear. Disseminated choroiditis with areas of pigment heaps and atrophy above and to the nasal side above the disk; the temporal half of the nerve was pale. In the left eye there were large sheetlike opacities with areas dense white in color and a hole in the center through which the fundus can be seen, with guy ropes and new-vessel formation and fine branching of vessels in the sheets; also a large area of choroiditis with atrophy and pigment heaping up and in from the disk. The laboratory and blood analyses were negative. There was no history of any injury to the eye. The fields were taken by Dr. Plumer, intern at the hospital.

## Bilateral Exophthalmos Due to Metastatic Osteosarcoma

Dr. Frederick Krauss reported a rare case of bilateral exophthalmos due to a metastatic melanotic, round-cell sarcoma, probably originating in the adrenals. The symptoms began with distress in walking, developing into a paraplegia about three months later, almost coincident with an increasing exophthalmos. The bilateral exophthalmos lasted about three months, gradually resulting in dislocation of the eyeball. The eyegrounds were normal for several

months, when optic atrophy slowly appeared, probably caused by the prolonged stretching of the optic nerve. The cornea slowly melted away, as in keratomalacia, about three weeks before his death. The patient's intellect, aside from deafness and blindness, was normal. At postmortem the entire interior of the skull, the external layer of the dura and the orbit showed new-bone formation in the shape of innumerable crypts and stalactites, with the interspaces filled with round-cell, soft, sarcomatous masses. The ribs, vertebra and femur, as well as the liver, left adrenal gland and left kidney, contained sarcomatous masses.

### Endothelioma of the Pituitary Body

Dr. William F. Bonner (by invitation) presented a case of endothelioma of the pituitary body with the following interesting features: (1) Normal field in right eye and atypical field in the left eye at first, later assuming bitemporal hemianopsia; (2) normal physical examination; (3) *x*-ray showed absorption of sella tursica; (4) diagnosis of neoplasm of the pituitary body by Dr. Charles H. Frazier, who did a transsphenoidal operation; (5) diagnosis of section made by Dr. Allen J. Smith as endothelioma; (6) improvement of vision and field in right eye; none in left eye.

### Gonioscopy and its Clinical Applications

Dr. M. Uribe-Troncoso, of New York (by invitation), described a new instrument, the "gonioscope," which he had devised to be used in conjunction with Koeppe's contact glass. It is a microscope and a periscope combined and gives magnifications of 10 and 20 diameters. A small electric lamp, supplied by a dry battery contained in the handle, gives the necessary illumination. The tube of the microscope is at right angles with the handle and is always held in front of the patient; the rays of light coming from the angle and parallel to the iris surface are deviated by a square prism and sent to the observer's eye in front. The microscope is revolved on its axis for the examination of the angle of the anterior chamber all around the limbus. Focussing is made by moving the tip of the instrument back and forth from the eye.

Goniscopy, like ophthalmoscopy, needs a complete training both

for obtaining a clear angle image and for making a correct interpretation of the findings. In the physiologic angle the following parts must be systematically recorded: (1) The pupil with the slope of the pupillary zone, the ridge of the lesser circle and the pupillary crypts; (2) the surface of the iris with the contraction folds and iris processes or spurs; (3) the ciliary border or visible limit of the iris, which is not the root of this membrane but the last ridge in the surface, the insertion of the root being made to the ciliary body directly underneath this ridge; (4) the ciliary body, which appears as a narrow, dark-brown stripe; (5) the sclerocorneal trabeculum covering the Schlemm canal, which looks generally as a grayish band separated at times from the ciliary body by a brilliant white line, the scleral spur. The canal is normally filled with transparent aqueous and not with blood. This may be found in congested eyes or pathologic cases and shows as pinkish-red lines on the limits of the canal; (6) the inner parts of the scleral limbus, appearing as a white band separated by an indistinct margin from (7) the inner concave dome of the cornea, a bluish, semitransparent crescent; (8) the optical section of the cornea. The observer has the illusion of seeing a microscopic section of this membrane.

The ciliary processes and the orbiculus ciliaris as far as the ora serata can be seen where a coloboma of the iris (either by operation, injury or in congenital conditions) is present. The size and shape of the processes are variable. They look like teeth, rounded or pointed, or they may be quadrangular or triangular. Sometimes two or three rows can be detected. The color changes from dark brown to light brown, the interspaces being darker.

The author described cases of pigmentation of the angle of senile origin and of atrophy of the root of the iris and of the ciliary processes as a result of the atrophy of the uveal tract after inflammations or degenerations. In iritis, when the acute stage has subsided and the cornea and aqueous are sufficiently clear for the examination of the angle, there are generally found exudates covering the whole sinus of the chamber. In a doubtful case of subacute iritis of the eye, with negative Wassermann but with a history of lues, the examination of the other apparently healthy eye showed typical papula of the root of the iris, which disappeared after one week of luetic treatment.

In some cases of peripheral synechia the author found a yellowish-brown or grayish-red zone immediately bordering the attachment

of the iris to the sclera and dotted with fine grains of pigment. He considers this as the impression left by the root of the iris on the sclera when, by the action of eserin or by iridectomy, the peripheral synechia is detached in part, showing that the adhesion was not still permanent. The character of the border of the iris inserted to the sclera in incomplete peripheral synechia has been emphasized by Salzmann, who compared it to a range of mountains. The author, however, has found in many cases the border of the iris with a regular or slightly wavy outline. In one patient, by continued eserine treatment, the iris surface was thrown into large meridional folds which produced in the sclera deep indentations in the adhesion.

In one case of chronic congestive glaucoma, with restricted synechia in the right eye and complete adhesion in the other, iridectomy performed in both gave good results in the right eye, while in the left the tension remained high and even a subacute attack of glaucoma came later, making a trephining necessary. Gonioscopic examination after the iridectomy showed small and atrophic ciliary processes in the right eye, while in the left the processes were swollen and the interspaces between them reduced. The same condition of the ciliary processes was found in another case of simple glaucoma with congestive attacks, where a trephining with partial iridectomy failed to lower the tension.

The author emphasized the scope and value of gonioscopy in all diseases affecting the iris root and ciliary body, as well as in congenital malformations and injuries. Thirty colored figures of normal and pathologic angles were shown.

Discussion. Dr. H. Maxwell Langdon said that he was interested particularly in Dr. Troncoso's statement that the gonioscope showed atrophy of the ciliary processes in the case where iridectomy had been successfully performed, but no atrophy in the case of unsuccessful trephining. He inquired of Dr. Troncoso if atrophy of the ciliary processes allowed better filtration. If this were true, it would appear that iridectomy is desirable. As iridectomy has always been an operation which tended to restore the normal physiologic course of the aqueous, whereas trephining created a new channel for its exit from the eye, the size of the ciliary processes would apparently therefore make little difference.

## APRIL 16

### Exhibition of a Case of Pit of Optic Nerve Head. Partial Coloboma

Dr. J. S. Plumer (by invitation) exhibited a colored woman, aged twenty-six years, with congenital cupping of papilla in right eye and partial coloboma in "pit" of papilla in left eye. Vision = 6/6 in each eye, with correction. Tension normal. In the right eye the vessels emerged from beneath the overhanging margin of the cup above, to the nasal side and below. The cup edges did not extend to disk margin as is noted in glaucoma, nor was arterial pulsation present. These conditions, according to Ball, characterize congenital cupping of the papilla. The remainder of the fundus was normal. The left eye revealed a deep, vertically oval, physiologic cup sloping into a small, deep, dark-gray pit at the lower margin. The central vessels were displaced somewhat upward. From the lower margin of pit there emerged a cilioretinal vein and also a leash of arteries and veins showing marked perivasculitis, the latter connected with the central vessels above by a small vessel running along the bottom of the cup and pit. The central vessels showed an anomalous arrangement. Otherwise the fundus appeared normal.

Fields, taken three times over a period of three months, showed in the right eye, a slightly enlarged blind spot, but color and form fields normal. Left eye, upper nasal quadrant cut, combined with Bjerrum scotoma due to involvement of inferotemporal fibers in the congenital disk defect (pit of papilla).

According to Dimmer, pitting of the optic papilla consists of round or oval areas, dark gray to black or green-blue in color, situated almost always in the lower temporal half, rarely in the lower nasal half, of the otherwise normal papilla. It varies in size from one-fourth to one-third the size of the papilla. The color, according to Lindahl, is due to shadows resulting from the presence of semi-transparent tissue. According to Lauber, pit of papilla is similar in nature to partial coloboma, on the basis of his findings histologically in one case. Some cases have emerging pit vessels, others none. Variations in details of appearance and arrangement of vessels is common. The condition of partial coloboma or pitting of the papilla is of uncommon occurrence.

Discussion. Dr. William Zentmayer stated that the presence of a cilioretinal vessel emerging from the pit is interesting because some one has suggested that this anomaly may be atavistic. In some of the lower types the retina is supplied by the ciliary circulation, the vessels entering the eye in a similar way. That this anomaly is closely allied to a coloboma was shown by Lauber in the study he made of such an eye. He found an invagination of atypical retinal tissue filling the floor of the cavity.

## Exhibition of a Case of Traumatic Retinal Lesion

Dr. Warren S. Reese exhibited a case of retinitis in a man, aged thirty-two years, who complained of poor vision in the right eye due to a bursting shell and bromide gas in October, 1918. He stated that he had been studied carefully at Fort McHenry and Johns Hopkins Hospitals, several years ago, for some systemic cause of his eye affection, but that nothing had been discovered. Externally the eye was negative. The opthalmoscope revealed a circular, yellowish, wreathlike lesion, horizontally oval and about 2 d.d. in diameter, with a small red dot in the center. The disk was hyperemic, with blurred edges, and the vessels exhibited perivasculitis, especially to the temporal side near and beyond the lesion, where there were a number of rather small, though variously-sized, pearly white and slightly refractile spots, usually arranged along the course of a vessel. In the lower periphery there were two rather large pigmented areas. Although exhibited as a case of circinate retinitis, it is certainly not typical of this condition and was presented for diagnosis and comment.

Discussion. Dr. William Zentmayer, said that from cursory examination of the case the evidence of inflammation is more marked than one finds in circinate retinitis. There is undoubted subsiding papillitis. The belt has not the usual location and the component parts are more glistening than is usually seen in circinate retinitis. The changes at the macula appear to be also of a more inflammatory nature. It is possible that the injury he received to the eye explains the fundus picture. Another possibility is diabetes, as these changes are suggestive, and likewise a typical circinate condition is often found as a complication of diabetes.

## Changes in Aqueous under the Influence of Certain Drugs.

Dr. Francis Heed Adler (by invitation) gave the results of studies of the aqueous humor under the influence of miotics and mydriatics. The protein content of aqueous humor, like cerebrospinal fluid, is quite low, approximately 0.03 per cent. In inflammatory diseases of the eye, particularly in those affecting the anterior segment, the protein content is increased. This is analogous to the increase in protein in the fluids filling serous cavities—as the pleural, pericardial and peritoneal cavities—during inflammation. The bloodvessels, normally impermeable to protein, under those conditions which characterize inflammation allow the protein molecules to pass through their walls.

Studies on changes in protein content of the aqueous humor under experimental conditions have been made by numerous investigators, but the methods employed have, for the most part, been too inexact for the measurement of such small changes. Thus the refractometric and the micro-Esbach methods employed by Seidel and Wessely, respectively, were found to be totally unsatisfactory in the hands of the author. A nephelometric method, devised by Dennis and Ayer for the quantitative estimation of protein in the cerebrospinal fluid, was found to be far more accurate and was, therefore, used in carrying out the experiments described. A summary of the results obtained were: (1) Eserine increases the protein content when instilled into the conjunctival cul-de-sac. Atropine causes no regular change, but instilled prior to the eserine, successfully prevents eserine from increasing the protein content. (2) Removal of the ciliary ganglion, resulting in degeneration of the third nerve fibers, causes a definite decrease in the protein content for which no explanation has as yet been found. In these experiments eserine is still able to increase the protein content. It seems certain, therefore, that eserine, in increasing the protein content, does not act on the ciliary epithelium, as suggested by Seidel, but probably on the bloodvessels directly. Full details of the methods used and experiments performed are embodied in the complete article in the *Archives of Ophthalmology*, May, 1925.

## 1. A Case of Perforating Injury of the Ciliary Body. 2. Perforating Injury of the Globe. Foreign Body in the Orbit. 3. Further Report of Foreign Body in Choroid

1. Dr. H. Maxwell Langdon exhibited a case of perforating injury of the ciliary body in a woman, aged twenty-six years, who was first seen on March 18, 1924, with a history that a small piece of china from a shattered cup had flown into her face, cutting the left upper lid and producing some blurring of vision. There was a wound of the left upper lid near its center, about even with the tarsal cartilage and upper limbus of the globe; also a penetrating wound of the ciliary body and a small bead of vitreous showing at the mouth of the wound. The iris was quiet, the anterior portion of the vitreous contained some hemorrhage, but the rest of the media were clear and the fundus normal. The *x*-ray gave no shadow of a foreign body, but this was not conclusive evidence that nothing had entered the eye, since china is of the same penetrability as muscle and, therefore, in the body is not to be distinguished from it. The patient was put to bed, and atropine and bandage applied. In three days the lid wound had completely healed and in two weeks the eye was quite white. Sodium iodide was continued for some months, the vitreous haze gradually cleared, except for some specks in the anterior portion and vision returned to normal.

2. Dr. Langdon also showed a case of perforating injury of the globe and foreign body in the orbit. The patient, a young man, aged twenty-three years, was seen first on January 30, 1922, with a history that he was struck in the right eye about one hour before by a piece of steel. Down and out there was a small conjunctival hemorrhage with a cut in the sclera through the ciliary body, slight haze in the anterior portion of the vitreous up and out from the disk, and an area of choroidal disturbance about the size of the disk. *X*-ray examination showed a small foreign body in the orbit back of the optic nerve. A moderately severe irodocyclitis developed, which quieted down, but a granuloma formed at the site of the wound. At the present time, except for a small amount of vitreous haze and a scar in the choroid, the eye is normal.

3. Dr. Langdon also showed a case of foreign body in the choroid, in a young man into whose eye, about a year before, a foreign body had penetrated and lodged in the posterior portion of the choroid.

The vision was normal and the eye quiet. When he was shown at this Section, Dr. Sweet thought, since the man had normal vision, it might be better to allow the body to remain and possibly become incapsulated rather than attempt extraction, which would probably fail. The man went to California, the eye became inflamed and had to be removed by Dr. Frank. Apparently a uveitis developed with a certain amount of siderosis.

These cases are shown because they all are instructive. The first shows a wound of the ciliary body, a foreign body evidently penetrating into the vitreous but not passing through the sclera, as no evidence of a foreign body can be seen at the present time, and in spite of this wound of the ciliary body the eye quieted down and is a perfectly useful organ. The second case shows how, by chance, the vital structures of the eye can be injured and yet no loss in vision occur, and the third that in all probability no foreign body in the eye can ever be considered as unlikely to cause serious trouble, and that globes with foreign bodies in them, even though quiet and with good vision, will be possibly lost later.

Discussion. Dr. William Zentmayer asked if there was a subconjunctival hemorrhage present in the case of double perforation. This symptom is said to be diagnostic of double perforation. In 3 of his cases he found it present in but 1, so that the negative phase is inconclusive.

## A Case of Osteosarcoma of the Orbit

Dr. William Zentmayer reported a case of a boy, aged sixteen years, who presented an extreme degree of proptosis of the left eye, with papillitis. Vision = l.p. There was firm resistance to replacement of the globe. No pulsation. No bruit. There was a palpable mass in the anterior portion of the orbit, both inferior and superior. The *x*-ray, made by Dr. Pfahler, showed a marked enlargement of the eyeball. After a course of *x*-ray an exploratory incision was made along the floor of the orbit. Through this a tumor could be felt below the optic nerve. Because of this an exenteration of the orbit was done. A dumbbell-shaped, dense mass, with the larger sphere above, was found to encircle the optic nerve. The whole tumor, having distended the orbit in its growth, was larger than the external opening of the orbit and it was necessary to crush it and pry it out. Following the operation radium was applied within the

orbital cavity, granulation took place normally and, one year later, there is no return of the growth.

The histologic study, made by Dr. Case, showed the growth to be an osteosarcoma of varying density, some portions showing a cartilaginous phase of ossification, while others showed relatively hard bone. The sarcomatous element was of the spindle-cell variety.

Dr. Zentmayer commented upon the difficulty of diagnosis in such cases and said that in his experience palpation was often misleading. He cited several instances where distinct masses could be felt in the anterior part of the orbit, when the growth was either in the accessory sinuses or well behind the globe. He believed those possibly to be due to the engorgement of the orbital veins, with edema, and possibly an increase or displacement of the orbital fat.

In answer to a question by Dr. Frederick Krause, Dr. Zentmayer said that examination of the nasal sinuses was made by Dr. Skillern and no extension of the neoplasm into these areas was found.

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## OCTOBER 15

### Exhibition of Cases of Xerosis Conjunctivæ

Dr. Leighton F. Appleman presented a woman, aged twenty-seven years, who showed xerosis conjunctivæ. The lesions consisted of triangular white patches on the bulbar conjunctiva of each eye, most marked on the temporal side of the corneæ. The patches looked not unlike unglazed white porcelain. The conjunctiva had lost its shining, moist appearance and was covered with dry, white foam. This could be readily removed with a cotton-wrapped applicator, leaving the conjunctiva dry, somewhat toughened and of a dirty-white color, closely adherent to the globe. The condition had existed for about eight years, gradually becoming more marked. A culture of the secretion from these areas revealed a pure growth of xerosis bacillus.

This disease appears to be due to the drying of the epithelium, usually beginning in the exposed portion of the conjunctiva in the palpebral fissure. It is associated with a debilitated condition of the subject or to a deficiency in certain dietary elements. In the present

case no such condition appeared to be present. The fact that it occurred in one of her age rendered it rather unusual.

Xerophthalmia and keratomalacia usually occur in poorly-nourished children, and a very thorough study of this type of case was reported by Blegvad, in 1924, who called attention to fat-soluble A vitamin deficiency. He gathered 148 cases of xerosis conjunctivæ, of which 133 occurred in children and only 15 in persons over fifteen years of age.

Treatment has been without material improvement. The effect of radium or of vaccine is yet to be tried.

Dr. Francis Heed Adler exhibited a case of xerosis conjunctiva in a girl, aged six years, with duration of six months. Various local remedies had failed to make any impression on the growth. Smears and cultures from the growth showed the typical xerosis bacillus. In view of the fact that this is often associated with a vitamine deficiency, cod-liver oil was ordered and exposures of Finsen light locally will be tried.

Discussion. Dr. Burton Chance inquired whether the appearance of the areas in Dr. Appleman's case had altered much while under observation, as he had not seen the eyes until tonight since he examined her at the Wills Hospital. At that time he regarded it as a case of lymphangectasis. The areas were then not covered with the smegmatic substance, nor were they as extensive as they are tonight. He had to admit that the present appearance could not justify such a diagnosis as that which he had made. Although he had not seen such cases of xerosis of the conjunctiva as the two shown tonight, he had repeatedly had to treat xerosis of the cornea. In one case, a boy, whom he had shown to the Section, broad bands extended across the corneæ, totally obscuring the sight; but by the performance of iridectomies both above and below the bands, in the vertical meridians, useful vision was obtained through the colobomas. A peculiar feature of the xerotic area is the strangely serrated or herringbone outlines marking the surfaces. Such lines are distinct in the cases shown tonight and were pronounced in the corneal case cited.

Dr. William Zentmayer said that, many years ago, he saw a case of xerosis in the infant child of a medical friend, where a diagnosis of absence of pancreatic function was made by the late Dr. Starr.

The child died when about a month old, practically of starvation. No autopsy was made, so that the clinical diagnosis was not confirmed.

Dr. Edward A. Shumway said that Professor Fuchs, in Vienna, had had the opportunity of seeing many cases of xerosis of the conjunctiva in association with hemeralopia, and recommended as very efficacious the addition of liver to the diet.

### Ectropion of Lower Lid Corrected by Graft from Upper Lid

Dr. William Zentmayer exhibited a patient on whom he had corrected an ectropion of the lower lid, aggravated by a Maxwell operation, by using a skin-graft transplanted from the upper lid, according to the method of Wheeler.

### Two Cases of Contracted Sockets Operated upon by Method of Wheeler

Dr. J. S. Plumer exhibited 2 cases of reformation of contracted socket by the operation suggested by Dr. J. M. Wheeler. One case, a man, lost the left eye following ulceration and perforation of eyeball incident to chronic trachoma, and, owing to contraction of the socket, could not wear an artificial eye. A good, deep, lower cul-de-sac was obtained, with preservation of the caruncle. A month following operation the patient was able to wear an artificial eye with comfort, and a good cosmetic effect was secured.

The second case, a woman, aged thirty-seven years, lost the right eye at the age of two, following injury with scissors. Enucleation had been done shortly afterward. The socket showed a moderate degree of contraction, due chiefly to two broad, vertically disposed bands of scar tissue involving the conjunctiva of lids and fundus of socket in the inner and outer thirds. A reformed socket, smooth and entirely lined with graft, was obtained, with deep cul-de-sac, except at the inner third, where the graft did not adhere to orbital periosteum, due probably to insufficient radical dissection at this point. Aside from some upward rotation of cornea of artificial eye, the result was satisfactory as regards the retention of the prosthesis. The cosmetic result could be improved by having a special prosthesis

made. Slight postoperative contraction was seen, but not enough to endanger the desired result.

It is important, as emphasized by Wheeler, that there be wide dissection with removal of all scar tissue, thinning of lids, intact Ollier-Thiersch (dermal) graft, smoothly covering a properly fitting, large stent, proper pressure dressing and careful postoperative care.

## Tuberculoma of Iris and Ciliary Body

Dr. Burton Chance exhibited a young girl, aged eleven years, with tuberculum of the anterior segment of the globe treated by injections of tuberculin, who was shown at the meeting of the Section in the spring, at which time there were present in the angle of the anterior chamber of the right eye six distinct tubercular masses, one quite large mass pressing against the cornea. These masses had their bases in the ciliary body and extended over the face of the iris. The pupil could be expanded somewhat, but the deeper media were too cloudy for definition of the fundus. There were deposits on the capsule and on the endothelial surface of the cornea. Under injections of tuberculin the ciliary region is free apparently from the nodular masses, although iris has become degenerated and adherent to the lens, so that no reflex from or view of the fundus could be obtained. Light perception was preserved. The left eye has not been affected and there have been no signs of general tuberculosis. The initial dose of O T was $\frac{1}{500}$ mg., continued until October 10 (at which date $\frac{1}{250}$ mg. was the dose). At no time was there any marked reaction; once the temperature reached 100.2°, at another 100.3° F.

This case is in marked contrast with that of a young mulatto woman shown to the Section a year or so ago, in which so violent a reaction followed the cautious injection of $\frac{1}{10000}$ mg. that the ocular signs rapidly increased, the masses seeming to have grown larger overnight, and the onset of glaucoma demanded the immediate removal of the globe.

## A Case of Tuberculous Keratitis

Dr. Warren S. Reese exhibited a girl, aged five years, with a definite family history of tuberculosis. She had tuberculosis of the right hip eighteen months ago, the hip now being ankylosed. The right eye presented a number of variously-sized infiltrates in different

layers of the cornea, most of them being deep. These are mainly in the lower third of the cornea and have the peculiar mutton-fat appearance that is so characteristic of tuberculosis. There is a posterior synechia up and in, but little inflammatory reaction. Since first seen, late in September last, the condition has shown little change. Tuberculin was not used. Dr. Ralph Tyson, who kindly saw the case, advised against it, fearing that it might stir up the hip condition, which is now quiescent. He hopes to arrange for heliotherapy in the near future.

## Muscle Recession for Correction of Squint

Dr. Warren S. Reese reviewed the various operative methods of correcting squint and called attention to the shortcomings of tenotomy. He proposed an operation in which the tendon is severed at its insertion and sutured to the sclera back of this point, a new insertion being thus effected. Three consecutive cases were briefly described and conclusions drawn as to the advantages of the procedure, especially when combined with some operation on the antagonistic muscle of the same eye.

## A Case of Retinal Degeneration

Dr. William Zentmayer exhibited a girl, aged twenty-one years, with a history of gradually failing vision unimproved by glasses. There was no headache, no mist before the eyes and no pain. Sight was poor at school and tests then failed to improve the vision. She is in apparently good health. She had a very severe case of whooping-cough at eight years of age, followed immediately by measles. In the same year she had mumps, with abscessed ears. She had never been seriously ill otherwise and has never had scarlet fever. The family history is negative, except that a paternal grandparent suffered from diabetes and that a brother died of tuberculosis of the throat, but there had been very little exposure at any time and none after he became actively ill. There was no record of blindness or hereditary eye-trouble and no blood relationship in parents or ancestors. V.O.D. = 3/80; O.S. = 5/9. Light sense, O.D., 0.8; O.S., 0.9. In the right eye the papilla was nearly round, with medium-

sized excavation. In a broad zone encircling the papilla and macula there are crescentic, round and macular-shaped, pale-yellow lesions from one to several times the diameter of the central artery. In the vicinity of the temporal vessels they coalesce to form continuous bands. They lie altogether beneath the retinal vessels and are less conspicuous along the inferior vessels. There is no pigment either in relation to the spots or elsewhere. There are pale, not very definite changes at the fovea. The outer half of the papilla is gray and the vessels possibly a trifle reduced in diameter. The same general appearance in the left eye, although the lesions are not so pronounced and show less tendency to linear formation.

This patient presents a retinal picture which does not conform to any typical form of degeneration with which we are familiar, but resembles an atypical circinate degeneration or retinitis circinata, described by Bachstez and Harms, in which the zone affected has for its center some other point than the fovea. Whether this is actually a case of so-called retinitis circinata may be questioned. In retinitis circinata the disease occurs usually in the middle or in the advanced years of life and is more often unilateral than bilateral and the lesions have a more definite, limited and characteristic configuration than the case exhibited, at least in advanced cases.

The points in which it resembles circinate retinitis are that the component lesions are yellowish or creamy, are small and well-defined, are situated beneath the retinal vessels and show a tendency to confluence and in mass to follow the temporal vessels. No pigmentation is present. There is likewise an indefinite, yellowish macula area. Central vision is greatly affected; the peripheral field shows little change and there is a relative central scotoma. There is no night-blindness.

Dimmer, who has described the variations which have been met with in the outstanding feature of the fundus changes, states that the girdle shows many variations in its composition, form and relation to the macula. At times spots of the same color and form are found outside of the girdle, even in the nasal part of the fundus, thereby greatly modifying the ophthalmic picture. The girdle does not always end at the disk, but may reach above and below the vertical diameter or even circumscribe it, reaching the nasal fundus, so that the papilla comes to lie within the girdle. This is the distribution in the case here shown.

Discussion. Dr. H. Maxwell Langdon said that although the case of retinal degeneration was not typical of circinate retinitis, it was not typical of any other form of retinitis. The idea occurred to him that it might be a form of retinal degeneration in which pigment migration had not yet started. It may be that these forms exist at least for some time before there is sufficient breaking down of the cells to allow the pigment to wander from its normal position.

Dr. Zentmayer stated that there was a slight deficiency of the light sense, which would of course tend to confirm his diagnosis of retinitis carcinata.

## A Case of Probable Pemphigus of Conjunctiva

Dr. William Zentmayer exhibited a case of pemphigus in a male, aged forty years, who was seen at Wills Hospital, September 4, 1925. The disease appeared two years previously, when both eyes began to itch, especially inside the lower lids. Some redness was noticed. These symptoms were intermittent, but grew progressively worse until about one year ago. Since then there has been little or no change so far as he can tell. About the same time that the eye symptoms began, the patient noticed that his nostrils were filled with crusts a great part of the time, causing considerable difficulty in breathing, which was more marked at night. In the right eye the sac was negative; the puncta somewhat small; there was some loss of cilia of lower lid, which are irregularly placed; there were a few very small patches of xerosis at outer third of inner border of lid with almost complete obliteration of cul-de-sac by adhesions between palpebral and ocular conjunctiva; moderate injection extending upward to lower limbus; with patchy scarring of conjunctiva of upper lid with bands on either extremity of tarsus extending to bulbar conjunctiva, giving the appearance as if the tarsus were being snared off; slight injection of bulbar conjunctiva; the cornea was clear; the anterior chamber was of the average depth; the pupil was round and reacts to light and convergence; the media was clear and the fundus negative. The left eye showed some loss of cilia of lower lid; obliteration of lower cul-de-sac except for the middle third, which is moderately shallow; there were pearly white patches of xerosis between the outer third of the lower lid

border and the cornea; a grayish-red membrane covered the outer fifth of the cornea from one to five o'clock; there was considerable thickening and scarring of the conjunctiva of the upper lid similar in appearance to that of the right eye. Pupil normal, but smaller than that of right eye. Media clear and fundus normal. The laboratory report showed no skin manifestations of pemphigus, but the nasal lesions suggestive of lues. Wassermann ++++. Differential blood count: Polymorphonuclears, 65 per cent; lymphocytes, 25 per cent; mononuclears, 3 per cent; eosinophiles, 2 per cent; transitionals, 2 per cent.

Pemphigus of the conjunctiva is a rare disease. In the past thirty years I can recall but 2 or 3 cases shown at this Section, and this is the only case that I have had in my practice.

Aside from the absence at the present time of vesicles, the symptoms both subjective and objective are those of pemphigus. The membrane forming at the outer part of the cornea in the left eye is probably the beginning of a process which may in time involve the entire surface. Little mention is made of the condition of the palpebral conjunctiva in the description of the disease. In this patient there is decided thickening of this portion of the membrane with dense cicatricial bands running transversely across the tarsus.

Eberson claims to have isolated an organism from the blood of 7 patients suffering from general pemphigus and this has held out a hope that the same organisms might be found in the blood of patients with ocular pemphigus. Dr. Kolmer, however, states that repeated efforts on his part to corroborate Eberson's finding have all failed.

Several of the cases reported have had positive Wassermanns, as in this case. It may be that syphilis is a contributing cause of this condition, as St. Martin claims that these patients are all syphilitic.

Stieren believes that pemphigus and essential shrinking of the conjunctiva are different diseases. He says that the palpebral conjunctiva rarely suffers in pemphigus. Some dermatologists contend that skin pemphigus and conjunctiva pemphigus are different diseases.

Benedict claims to have obtained benefit for some of the symptoms by using a vaccine of the xerosis bacillus taken from the conjunctival exudate. In some instances radium has been of apparent benefit.

Discussion. Dr. Langdon thought the second case presented by Dr. Zentmayer undoubtedly one of pemphigus of the conjunctiva. He had seen 2 cases, 1 of which was under his care now, and both of them have had general as well as ocular involvement. Inasmuch as many of these cases have general involvement it seemed to him rather peculiar that Dr. Schamberg believed that pemphigus of the conjunctiva and general pemphigus were two separate conditions.

Dr. Langdon said that, a year ago last June, at the meeting of the American Ophthalmological Society, Dr. Benedict, of Rochester, Minn., in discussing Dr. Clapp's case of pemphigus, mentioned that in certain cases of his own xerosis bacillus had been found in great numbers, from which a vaccine was made and used to advantage. It occurred to him that if a vaccine would ever be useful it would be in cases like Dr. Appleman's and Dr. Adler's.

Dr. Edward A. Shumway said that he had seen 3 well-marked cases of pemphigus of the conjunctiva and in only 1 was there any skin involvement, which tallied with the usual experience in these cases, mucous membrane involvement of the nose and throat being the much more common accompaniment. In 1 case syphilis was present and he thought this was an important factor, as the pemphigus might be a late manifestation of this disease and appropriate treatment against it should be instituted. In 1 of his patients there had been involvement not only of the mouth and pharynx, but also of the mucous membrane of the bladder.

Dr. William Campbell Posey thought the case one of essential shrinking of the conjunctiva. This condition must be differentiated from that of pemphigus of the skin with ocular manifestations. He had recently reported a case of this latter type in an asthenic individual who had recently died. This characteristic of ill-health is a dominant feature in the skin disease. The long duration of the affection, in the case under discussion, without corneal complications is against it being trachoma. The history was negative regarding the possibility of any burn of the conjunctiva by cauterizing agents. He had seen but one other instance of essential shrinking of the conjunctiva in his practice.

Dr. Burton Chance said that he had observed several cases of pemphigus and would not class Dr. Zentmayer's case as trachoma-

tous, although he was at a loss to account for the free discharge collected on the tarsal structures.

Replying to Dr. Langdon, Dr. Zentmayer said that it is because ocular pemphigus is so rarely associated with skin pemphigus that the doubt as to their being the same disease exists. A less forcible reason advanced is that patients with skin pemphigus usually die of the disease, whereas there is no mortality in ocular pemphigus. The patient exhibited is receiving active antisyphilitic treatment and under the care of Dr. Lane radium is to be tried. In regard to Dr. Langdon's thought in the case shown as circinate retinitis, he believed that were it an early stage of retinitis pigmentosa there would be night-blindness, which is not present although there was insignificant diminution of the light sense; also the peripheral field was normal in extent.

## Result of Ziegler Through-and-through Operation for Traumatic Cataract

Dr. L. Waller Deichler exhibited a case in which a V-shaped through-and-through Ziegler operation was done for traumatic cataract with excellent results. The history of the case was as follows: Mr. J. K., aged thirty-seven years, an electric welder, gave a history of a piece of steel penetrating the left eye on December 9, 1924. The steel passed completely through the lens, lodging in the vitreous 10 mm. below the horizontal plane, 7 mm. to the temporal side of the vertical plane and 8 mm. behind the center of the cornea. This was removed on March 7, by the Sweet magnet, through an open incision in the sclera as near the foreign body as possible. Healing without complication ensued, and on April 18 a V-shaped through-and-through Ziegler operation was done for traumatic cataract. Convalescence was uncomplicated, and six months later, with lens correction, vision = 20/20 partly.

Dr. William Zentmayer said that he was a friend of the operator, but he thought it should be stated that occasionally there is a marked reaction. In one case, already mentioned in discussion, it was quite severe. Furthermore, increased tension frequently occurs. The patient should not be discharged too early in the belief that this complication does not arise.

Dr. S. Lewis Ziegler said that the principle of complete discission applies to traumatic cataract just as well as to any other type of soft cataract. In order to escape all postoperative trouble it is only necessary to freely open both the anterior and the posterior capsule and to avoid any injury to the iris or to the ciliary body.

## Retrobulbar Neuritis Followed by Optic Atrophy Due to Frontal Sinusitis

Dr. L. Waller Deichler presented the case of a man, aged forty-two years, who showed true retrobulbar neuritis, followed by progressive optic atrophy. Vision upon examination was R.E. = 14/40, improved with glasses to 15/15; L.E. = 20/200, unimproved with glasses.

Fields, however, for both form and color were slightly contracted in the right eye, but markedly contracted in the left. There was a large relative scotoma for green in the right eye and in the left eye an absolute central scotoma for all colors and paracentral scotoma for red and a relative scotoma for green. Laboratory analyses, both for urine and blood, were negative. Normal pituitary. X-ray of teeth showed two abscesses. Following removal of the teeth, vision improved to 15/70. As he had had acute ethmoidal disease of the left side two months previously, both ethmoids and sphenoids were opened, but no pus was found. Vision, however, improved to 15/40. The contraction of the fields continued, with almost complete loss of nasal field in left eye. He developed symptoms of left frontal sinusitis, and a modified Killian operation was performed. Immediate improvement followed, and vision increased to 15/15 partly, with peripheral field restored to two-thirds of normal.

Discussion. Dr. Robert J. Hunter said that this case illustrates the benefit that may occur in retrobulbar neuritis when a distant source of toxemia is removed, such as teeth; from depletion after operation on the normal posterior ethmoids; and from removal of the focus in the frontal sinus.

## Relation of the Aperture of the Eye to Ocular Function

Dr. Alfred Cowan gave a demonstration on an optical bench of the effect of the various shapes and sizes of stop-aperatures on the image when in focus, with comparison between this simple system

and an emmetropic eye, which showed that good vision does not depend on the size, shape or position of the pupil. He also showed the effect of a stop-aperture when the image-screen does not lie in the focal plane, with illustration of diffusion images in ametropia, showing that the vision of patients with irregular or displaced pupils or opacities in the media may be lowered out of proportion to the refractive error.

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## NOVEMBER 19

### A Case of Incomplete Remains of the Hyaloid Artery

Dr. Burton Chance exhibited a case of hyaloid artery. The tube was not complete although it extended far forward, terminating in a hooklike thread. There were no other vestigial remains or anomalies. The man had served in the army, and stated that he had been credited with full acuteness of vision at every examination during his service. Within the past year the sight of his left eye had failed without any known cause. Uveal pigment was present in fine spots on the lens, and a two-celled area of choroidal atrophy below the macula, with the vitreous so fluid that the hyaloid tube floated about on movement of the globe. Undoubtedly an insidious uveitis caused the loss of sight. The man has been under observation for so short a time that his case has not been studied fully, but was exhibited as a matter of general interest only.

Discussion. Dr. William Zentmayer said that he had recently seen a case of complete retention of the hyaloid artery, the first one since acquiring the slitlamp. Ophthalmoscopically the vessel seemed to be complete. With the slitlamp the greater portion of the posterior capsule between the center and the periphery was seen to be covered by an outspreading, white, fibrous-like mass with numerous lacunæ. From this the extension backward could be traced for about one-third of the vitreous. Despite this anomaly the patient had normal vision.

Dr. Luther C. Peter stated that through the courtesy of Dr. Zentmayer he had had the opportunity of examining the case to which Dr. Chance referred. It was not possible to follow the hyaloid

artery by means of the slitlamp for more than one-third of its length posterior to the lens capsule, although with the ophthalmoscope it could be followed close to the disk.

## Plastic Correction of Cicatricial Ectropion

Dr. George H. Cross presented a case showing the results of plastic repair of the eyelids to correct cicatricial ectropion. The patient, a man aged fifty years, was severely burned with a caustic solution, sodamite. The whole face and the entire left side of the head were involved. The repair of the left upper lid was by a "Gilles outlay," while the right upper and left lower lid were treated by first dissecting the lid loose and then putting it on a stretch by suturing the edge to a piece of adhesive plaster applied to the face. The thin Thiersch graft from the arm of the patient was then placed in position to cover the raw surface and the whole covered with a layer of Kerr's modeling compound. A bandage was applied with firm, even pressure for six days. The correction of the left lower lid was undertaken just thirteen days ago. Special attention was directed to proper separation of the completely ectropionized eyelid from the cheek by blunt dissection in the area of facial attachment, or what may be called the line of cleavage. This permitted the return of the lid, undamaged except for the loss of the surface epithelium, to its proper place, and aided the return of function, which took place after the surface grafts had healed.

The case illustrated the advantage of extremely thin epidermal grafts. Their color blends with the surrounding tissue so that it is difficult to find the line of demarcation of the graft. When thicker grafts are used there is a marked color difference, with the edges sharply defined.

Discussion. Dr. Wm. Campbell Posey said the case recalled that of a man with an extensive burn of the face resulting in ectropion of all four lids. Grafts to overcome all these deformities were employed at a single operation. The grafts in the upper lids took, those in the lower sloughed. As the patient was enabled to wink by reason of the restoration of the upper lids to their normal position, he was so satisfied that he permitted the eversion of the lower lids to go uncorrected. An interesting feature of this case was that, although the patient was a driver, and notwithstanding his inability

to wink, he has gone twenty years without suffering any loss of visual acuity, although the epithelium of both cornea was somewhat hazy.

## A Case of Congenital Bilateral Symmetrical Downward and Inward Dislocation of the Lenses

Dr. William Zentmayer exhibited a case of congenital bilateral symmetrical downward and inward dislocation of the lenses in a young girl, aged seven years, whose father had a similar malformation. Vision: right eye = 3/60; left eye = 4/30. The lenses were slightly cloudy, but showed no localized opacity. Three discissions had been performed on the left eye, and the lens was now opaque, with fragments of cortex in the anterior chamber. The operation had been undertaken because of the low vision and the possibility of secondary glaucoma later in life. Discission was chosen as being the safest. It is difficult of performance, as the lens has no attachment above and backward dislocation may result in the attempt to open the capsule.

A recent case was cited of a young man, aged sixteen years, who had a similar anomaly with hypertension. A simple extraction was safely accomplished in one eye with a resulting active, round pupil. Encouraged by the successful result, the other eye was similarly operated upon and lost through iridocyclitis, resulting in atrophy of the globe.

Discussion. Dr. S. Lewis Ziegler said that about twenty-five years ago he showed before the Section a case of double dislocation of the lens. The cataract was held by a single attachment up and out. He performed complete discission by entering the knife-needle below the center of the cornea, puncturing the lens with a quick thrust near its center and cutting downward and inward through its free periphery. This cut was repeated in a second direction, so that the cortex was freely exposed to the aqueous. Dissolution was very rapid, there was no reaction and the capsular remains retracted from the pupillary area. The visual result was considerably better than the preoperative test for aphakia which had been made over the free lens margin, under full mydriasis. He recently learned that the patient had maintained this good vision all these years. He thought complete discission is much to be

preferred over the loop, since the lens is usually of jellylike consistence and the peripheral adhesion is sometimes so firm as to cause ciliary traumatization when the lens is looped. Where, however, the lens is wholly dislocated he believed nothing was superior to his barbed vectis, since it takes hold firmly and retains its grip on the lens until it is extracted.

Dr. Wm. Campbell Posey said he had removed such dislocated lenses both by the loop and by the needling. He had been able by the first procedure at times to extract the lens without loss of vitreous and with favorable visual results. In other cases he had not been so fortunate. When needling he first endeavored to control the movements of the lens by transfixing it by means of a needle thrust posteriorly to the lens through the sclera, another needle being used to enter the lens through the cornea, as usual.

Dr. George H. Cross said that he had operated a short time ago on a girl, aged eight years, with a double congenital dislocation of both lenses, the dislocation of the lens in the right eye being outward and in the left eye upward. Vision: right eye = 20/200; left eye = 20/100. The choice of operation was influenced by the bad results following a needling seen a short time ago in the case of a young boy who eventually lost his eye. Although this was not a case of his own, its influence decided him against a needling and in favor of removal by a loop. The right eye was selected for operation, as it had the poorer vision. No vitreous was lost and the case recovered nicely. A van Lint flap had been prepared as a precautionary measure and was sutured in place following the extraction of the lens.

## A Case of Paralysis of Downward Movements and of Convergence

Dr. Warren S. Reese exhibited a case of paralysis of the downward movements and of convergence in a man, aged twenty-two years, first seen July 13, 1925. The following history was obtained: In January, 1923, he began to see double. This lasted two weeks and then both lids drooped. Ptosis lasted two weeks, and when it cleared up he could not look down or see near objects. His chief trouble now is that he gets sleepy and has difficulty in walking, as he cannot look down. Examination showed slight ptosis of the left

upper lid; lateral ocular movements good; upward movements limited and downward movements abolished, the patient being unable to move his eyes at all below the horizontal plane. There is no convergence power and some limitation of adduction of the right eye. Fundus examination negative. The patient requires sph. +2 lens in front of O.D. to reach 1M print at 7.5 inches; with the left eye he could read this print at 9 inches without the sphere. The case is shown not only because of its rarity but to direct attention to certain ocular complications of encephalitis lethargica which have not received the attention they deserve. These include affections of the upward and downward movements, of convergence, accommodation and divergence. Convergence is frequently affected.

Apparently nothing definite is known of the location of the lesion in these cases. He had talked to several neurologists especially as to whether the lesion was nuclear or supranuclear. Personally he felt that the lesion must be above the nuclei. If there are centers for these functions, clinical evidence seems to indicate that those for convergence, accommodation and upward and downward movements must be close together, while divergence has a separate and distinct center. The pupillary reactions in this case seem to suggest that the contraction of the pupils for near is a convergence rather than accommodation reaction. A case of convergence paralysis that he reported two years ago seemed to bear this out, as does also a case cited by Parinaud.

Discussion. Dr. William Zentmayer said that twenty years ago he published a case of paralysis of the upward movements of both eyes and weak convergence in a man of alcoholic history. The case was also seen by Dr. Spiller, who likewise considered it to be one of associated paralysis of the upward movements. However, in the course of a week's time the man developed diplopia and recovered rather rapidly the function of the individual muscles separately. This required a revision of the diagnosis and location of the lesion. It was considered at first to be a case of Wernicke's encephalitis superioris; Dr. Spiller decided that the lesions must have been in the third nuclei in the aqueduct of Sylvius. The center for convergence seems now to have been located between the nuclei of the third nerves in the median raphe, between the posterior longitudinal bundles. It is considered by some that a loss of convergence always accompanies paralysis of the associated upward

and downward movements of the eye in the primary position, but may be retained in the associated lateral movements.

Dr. Luther C. Peter said that the loss of associated movements upward, downward and in convergence, independent lateral movements good and full in each eye, and elevation and depression of each eye separately better than binocular movements upward and downward, would seem to indicate nuclear involvement as well as a supranuclear lesion along the aqueduct of Sylvius in the posterior longitudinal bundles.

Dr. H. Maxwell Langdon said that one of the most interesting things about the ocular complications of lethargic encephalitis is the fact that such minute lesions can remain affecting so completely certain small portions of the nervous tract and not involve parts which are closely adjacent. In his own experience, considering the extraocular muscles separately and individually, he thought that paralysis of the ciliary muscle was perhaps the most frequent. He had seen loss of convergence alone in the case of a young woman attending the clinic at the Infirmary for Nervous Diseases, about two months ago. The conjugate deviation and uniocular rotations were normal, but the convergence was entirely abolished.

Dr. Louis Lehrfield said that he was preparing a report on five cases of postencephalitis, or Parkinson's syndrome, in which the conspicuous ocular finding was a conjugate deviation of the eyeballs upward. He regarded the symptoms at first as a palsy of the inferior rotators, but was later convinced that the upward rotation of the eyeballs was spasmodic, due to irritative changes in those nuclei of the brain generally affected in encephalitis. His conclusions were affirmed by nurses and orderlies that the upward spasm of the eyeballs of patients may be relaxed by distracting the patient's attention in various ways. The spasm also may be broken when the patient's attention is distracted in the course of eating. The patients themselves describe the spasm of the eyeballs as only temporary in character, sometimes lasting a few moments or several hours, and in one particular instance over a period of days.

Dr. Sidney L. Olsho said that while the obscure etiology of this patient's symptoms is being studied he would suggest that he be given such relief as would be afforded by prisms, 6 or 8 degrees, placed base down before the eyes.

Dr. Reese stated that he had intended to cite Dr. Zentmayer's case and to ask if it was a case of encephalitis lethargica. His experience has not been the same as Dr. Lehrfield's, in that these cases clear up. He understood, however, that these palsies are often transient during the acute stage, as Dr. Langdon remarked. He had not been fortunate enough to see these cases during this stage, however.

## Melanosarcoma of the Palpebral Conjunctiva

Dr. Wm. Campbell Posey reported a case of melanosarcoma of the palpebral conjunctiva illustrating the malignancy of such growths, occurring in a male aged fifty years. A small, pigmented, vascular tumor imbedded in the conjunctiva of the left lower lid had been successfully removed by desiccation ten years previously. The second malignant growth had appeared in the upper lid of the same eye ten months before the report was made, and took the form of a pedunculated, pigmented and vascular tumor arising from the fornix. Excision, followed by radium, effected the disappearance of this mass, but involvement of the lacrymal, preauricular and cervical glands of the same side followed. Notwithstanding excision of these tissues and the continuous application of radium, matastases occurred in the lungs and brain, causing death. Dr. Posey spoke of the rarity of sarcoma of the conjunctiva in general and of the tendency of the nævi of the conjunctiva to become malignant in later life, and he advised the removal of all such growths in patients over thirty years of age, or earlier if symptoms of malignant activity manifested themselves. He did not share the opinion of Verhoeff and Loring regarding the extreme malignancy of sarcoma of the epibulbar region, and did not think enucleation indicated in all such cases, good results often following less radical measures. He gave a report from the literature of a number of cases of sarcoma of the conjunctiva and of nævi of the conjunctiva which later became malignant.

Discussion. Dr. Burton Chance stated that he had always suspected that the small sarcomata might really be a part of a general sarcomatosis. He desired to record that the two persons from whose epibulbar regions he removed small sarcomas, which recurred twice after excision, but which were satisfactorily treated

by desiccation about twelve years ago, as reported at a meeting of the American Ophthalmological Society, are still alive and well and have exhibited no recurrence.

Dr. William Zentmayer inquired if it were possible that some of these cases of sarcoma of the conjunctiva are local manifestations of general sarcomatosis? This thought occurred to him because of the frequent systemic involvement which should not occur as a result of metastasis if the belief of Collins and others, as quoted by Dr. Posey, is correct, namely, that extirpation of the growth alone is sufficient to prevent metastasis.

Dr. S. Lewis Ziegler said that he had elsewhere referred to a case of melanosarcoma of the limbus that did not yield to desiccation, but did yield to the application of a pencil of carbon dioxide snow. Not only did the growth wholly disappear, leaving apparently normal tissues, but the melanotic deposit was gradually absorbed. More than two years had elapsed and there was no sign of a recurrence. The use of this physical agent ($CO_2$) requires one or two applications of from five to ten seconds each. There is some reaction, which is controlled by applying ice-pads for from twenty-four to forty-eight hours. After that, positive galvanism is maintained until the ocular tissues recover their normal appearance.

## Removal of an Epithelial Plaque at the Corneoscleral Junction by the Shahan Electrothermophore

Dr. G. Oram Ring gave the history of a man, aged sixty-five years, who consulted him last spring regarding a small sessile growth situated exactly at the inner corneoscleral margin of the right eye. He was without pain and the congestion surrounding the growth was exceedingly slight. Its presence had been noted for one week only. The corrected vision was normal. Wassermann negative.

The plaque was nearly round, slightly irregular at the edges, gray-white and about 7 to 8 mm. in diameter. It was somewhat elevated above the level of the corneoscleral tissue and strongly suggested a small patch of flattened, frozen snow, quiescent and attached to the region referred to. There was no history of traumatism and neither family nor personal history was suggestive and the ocular structures were otherwise normal.

Reference was made to the division of the blastoderm that concerns us in the study of ocular growths, namely, the cuticular epiblast, the neural epiblast and the mesoblast. With the cuticular epiblast our growth concerns itself, derived as it is from the surface epithelium, which after embryonal life ceases to prolong itself into the deeper mesoblast. When this characteristic is reversed at the junction of the cornea, malignancy is always to be feared. The work of Collins and Mayou was especially referred to, and it was found difficult to differentiate Dr. Ring's description from that of Mr. Treacher Collins, which follows: "At first an epithelioma of the surface of the eye forms a small, opaque, white, raised patch." Reference was made to the use of the word "plaque," as given in the *American Encyclopedia of Ophthalmology* and to that of Mr. Parsons in the *Pathology of the Eye.*

After cocainization of the eye and the instillation of a few drops of a sterile solution of adrenalin chloride, 1 to 5000, the thermophore at a temperature of 148° was applied to the growth for sixty seconds by means of a conductor with an 8-mm. contact surface. The application was made with the patient in a prone position, a 1 to 5000 sterile bichloride ointment applied and the eye bandaged for twenty-four hours. It occasioned little or no pain, and judging from the perfection of the result attained in this instance, as well as in the prompt improvement noted in a series of corneal ulcers in which he has since utilized the method, he regarded it as an exceedingly valuable adjunct to our ophthalmic armamentarium.

Discussion. Dr. Luther C. Peter said that he wished to add his testimony to that expressed by Dr. Ring, as to the value of the thermophore in the treatment of corneal ulcers of certain types, especially of the sluggish type, to which the ulcer yields so satisfactorily and promptly.

## Chancroid of the Eyelid

Dr. Leighton F. Appleman and Dr. S. S. Greenbaum reported a case of chancroid of the eyelid, in a negress, aged thirty-five years, who had received antisphilitic medication for four months previous to the appearance of the lid lesion, which consisted of a small pimple on the right upper lid, which broke down, forming a deep, tender and painful ulcer with sloping edges, grayish floor and soft borders.

The diagnosis was confirmed by smears, which showed the Ducrey bacillus upon microscopic examination. The Wassermann + 4. Physical examination revealed perforated nasal septum and perforated soft palate; also several painful ulcers along the urethral meatus, one of which had perforated the urethra. She had complained of burning upon micturition for one week previous to the eyelid infection. The eyelid lesion and also those around the urinary meatus cleared up very quickly under the use of hot compress and iodoform.

Herbert Parsons, in his *Pathology of the Eye*, states that Eudlitz (*Arch. gem. de med.*, 1897) found, of 66 cases of soft chancre of the head and face, only 3 cases on the eyelids. In looking over the literature in the *Ophthalmic Year-book*, no report of a similar lesion in this location could be found.

## A Case of Unusual Meningitic Anthrax

Dr. Frederick Krauss presented a case of anthrax apparently beginning in the right upper lid without the formation of any visible pustule. Death occurred from meningitis about one week after its onset. When first seen there was intense and dense swelling in the upper lid, extending into the soft tissues on the temporal side. The eye was normal, but seen only after forcible lifting of the lids. There was no break of the skin nor any visible macule. An incision was made in the swollen lids and a culture made, which was negative. Two days later the patient had a convulsion. Further smears and cultures were negative until the following day, when, after spinal puncture was made, pure anthrax bacilli were found in the spinal fluid. The postmortem changes were those of hemorrhagic meningitis.

## Heterochromic Cyclitis with Cataract Formation

Dr. John S. Plumer (by invitation) exhibited a case of heterochromic cyclitis with cataract in a man aged thirty-five years. The history showed that the cyclitis had developed insidiously and without subjective symptoms. A few small, discrete deposits were noted on the posterior surface of the otherwise clear cornea, unassociated with ciliary injection. Coincident with the cyclitis, a mature, densely white cataract developed, which had been extracted with

success. Examination of the iris with slitlamp disclosed pigmentary changes in the iris, with slight change of color.

Dr. Plumer added that the changes in heterochromia might be due to a primary absence of mesodermal pigment (chromatophores) in the iris and choroid, or as the result of a chronic inflammation in these tissues.

Discussion. Dr. William Zentmayer said, as he understood the classification, there was a group of congenital cases which showed no evidence of an active inflammatory process, although there was usually a slight deposit on Descemet's membrane if the cases in this group subsequently developed a low-grade cyclitis and cataract.

There is a second group which is associated with involvement of the sympathetic nerve. The first class should not be confused with the discoloration of the iris which takes place in an iridocyclitis and which we may also have as a sequel in the development of cataract. As he understood it, in the first group, there is not a depigmentation of the iris—certainly not in the beginning; but there is a lack of development of the chromatophores. It was not clear to him whether Dr. Plumer's case belonged to the first group or was one of complicated cataract following an acquired uveitis.

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## DECEMBER 17

### Paralysis of Downward Movements and Convergence Three Years after an Attack of Lethargic Encephalitis

Dr. Edward A. Shumway and Dr. Franklin L. Noyes showed a case of paralysis of downward movements and of convergence, with paresis of accommodation, three years after an attack of lethargic encephalitis. The patient, a boy, aged seventeen years, had diplopia from the beginning, and showed a masklike rigidity of the face, tremor of the right hand and distinct disturbance of mentality and disposition. The paralysis of downward movements and convergence was complete; there was some limitation of upward movements, especially of the right eye. Lateral movements were full and nystagmus was present. The vision and eyegrounds were

normal. Pupils were unequal and the reflexes were sluggish. Statistics showed that 45 per cent of cases of encephalitis showed involvement of the eye three years after the onset. Paralysis of convergence was the most common, occurring in 66 per cent, and paralysis of accommodation in 26 per cent. Associated disturbance of upward and downward movements, either singly or together, was quite common in the acute stage but was usually fleeting, and as a permanent effect was very unusual. Dr. Shumway discussed various theories as to the location of the lesions and said that the majority of authors placed them in the nuclei in the neighborhood of the corpora quadrigemina, with disturbance of the fibers of association between the individual nuclei, or between the nuclei and higher centers controlling the associated movements, which it seems necessary to assume. Where the paralyses are fleeting, the lesions may be cortical.

Discussion. Dr. Warren S. Reese asked Dr. Shumway whether in this case the pupils seemed to react more to monocular accommodation than to attempted convergence? He was interested to note in the last *Journal of Ophthalmology* that in a case shown before the Chicago Ophthalmological Society, Dr. Suker drew the same conclusion that he did in the case he presented at the last meeting of this Section, namely, that the reaction of the pupils, when looking at a near object, was more likely a convergence than an accommodative reaction. The difficulty of determining this definitely is that these cases usually have accommodation, as well as convergence, affected though not to the same extent.

Dr. Shumway, in reply, said the reaction of the pupils to light was very slightly sluggish and no reaction to accommodation could be detected.

## Juvenile Glaucoma

Dr. William Zentmayer exhibited a case of juvenile glaucoma in a male, aged twenty years, who was admitted to the Wills Hospital December 7, 1925. He stated that his vision had been good until three weeks previously. It is probable that the reason for limiting the poor vision to so short a time was the fact that at that time he applied for a change of glasses and found that the sight in the right eye was almost gone. He had slight pain in the right temporal region at times and occasional halos. His father had bilateral

glaucoma, for which operation was done. He believes his brothers and sisters have good vision. Right eye: Pupil was dilated to 9 mm. and was inactive. Cornea appeared clear and was anesthetic; the rest of the media was clear. There was an exceedingly deep glaucomatous cup and narrow halo about the disk. There was a spontaneous arterial pulse affecting almost the entire distribution. The veins were engorged, especially the superior temporal. Anterior chamber was very deep. Left eye: Sensibility of the cornea diminished; pupil, $2\frac{1}{2}$ mm.; iris prompt to light. There was no glaucomatous cup. The slightest pressure on the globe produced retinal arterial pulse. Anterior chamber deep. Vision: right eye = 3/60; left eye = 6/15. Tension: right eye, 65; left eye, 57 mm. Hg (Schiötz tonometer.) It was impossible to determine any field of vision for the right eye. Ten days later the tension in the right eye was 60 and in the left 51 mm. Hg, and the vision in the right eye 6/22, and in the left eye 6/5. The field in the right eye showed a quadrant on the temporal side, with preservation of fixation and slightly enlarged blind spot. In the left eye the field was concentrically contracted and the absolute scotoma of the blind spot was within normal limits, but there was a zone of relative scotoma of about 5 degrees around it. The Wassermann was negative. There was acute purulent ethmoiditis and diseased tonsils. Despite the use of 1 per cent solution of eserine the tension remains high, fluctuating between 63 and 75 mm. Hg in the right eye, and 38 and 57 mm. Hg in the left eye. It is contemplated to continue the eserine treatment and to have the ethmoidal and tonsillary inflammation attended to before operating upon the eyes.

These cases are quite unusual and this one is exceptional in the exceedingly high tension and unusual extent of the arterial pulse wave. The condition is hereditary and shows the phenomenon of anticipation.

There are some who believe that in cases of glaucoma in the young it is probably of a secondary nature, but this seems scarcely logical when one considers that this type of glaucoma particularly is likely to be hereditary. Nevertheless, there is a possibility that the general circulatory condition of the eye may be improved by removing the nasal and tonsillar foci of suppuration.

Discussion. Dr. Frederick Krauss felt that in all suppurative conditions the primary object to be accomplished is free drainage

as rapidly as possible. Nothing relieves acute or chronic suppurative sinusitis as quickly as surgical intervention. In view of the seriousness of the ocular condition in Dr. Zentmayer's case, it would seem that immediate action would be preferable to dependence upon medical treatment.

In closing, Dr. Zentmayer said that he quite agreed with Dr. Krauss that the proper treatment of purulent ethmoiditis was operative drainage, that any medical treatment given to accomplish what would only delay the inevitable.

## Bifocal Trial Case Lenses

Dr. J. Milton Griscom exhibited a set of ultex bifocal lenses designed to be used in a trial-frame in conjunction with the ordinary trial-case lenses. The bifocals were ground plain in the upper segment with plus sphere of varying strength in the lower segment, so that when placed in the trial-frame in front of the patient's distant correction he may have an approximate idea of the action of bifocals. Dr. Griscom had found this of great value when there was doubt in the patient's mind regarding the use of bifocals, and considered it a useful addition to his trial-case equipment.

Discussion. Dr. L. Waller Deichler said he wished to thank Dr. Griscom for calling his attention to what he believed would prove a valuable addition to his trial-case. Frequently he had been perplexed in the presbyopia, after the correction of the near vision, by the difference in the focal point with the lens in the trial frame and in the finished bifocal lens. Again, the question whether the patient, who has never worn a bifocal lens, will be happier in the finished product or with a separate pair of glasses for near work, has also proven perplexing. Then, too, during the examination of those accustomed to wearing bifocals, frequently there is shown a tendency to tilt the head backward, so that the lower portion and not the optical center of the correction lens is being used. While the use of a triple-cell trial-frame overcomes this to a definite extent, it is not always satisfactory.

Dr. J. Hiland Dewey said that the optician, William Darling, furnished him with similar lenses eight years ago, and he has found

them quite useful in demonstrating to the patient the difference in the addition for a reading glass and that which they might require for a vocational glass.

## Monocular Color-blindness

Dr. William F. Bonner stated that cases of monocular color-blindness recorded have been few in number. In cases examined by him, he noted the following varieties: Total monocular color-blindness; partial monocular color-blindness; binocular color-blindness caused by color-blindness of the eye of choice, but normal color-vision in the other eye when the poor eye is occluded. He felt that in all occupations requiring normal color-vision the eyes should be examined separately. Further, in that pathological conditions are often associated with color-blindness, the color-vision tests should be included in the oculist's routine examination. He also recommended examination of automobile drivers for color-blindness by reason of colored lights used as traffic signals.

Discussion. Dr. Burton Chance said he was grateful to Dr. Bonner for bringing up the subject of color deficiency manifested in the vision of one eye only, for such cases are extremely rare, if, indeed, it is possible for it to be present in one eye and not the other through congenital fault. Only about three times has it been reported. In his own experience, in a very large number of examinations, he has not recorded a single instance. It is his constant routine to examine each eye separately. Not seldom has he found marked variations in the color response of the two eyes. He was therefore of the opinion that had Dr. Bonner's case been subjected to varied laboratory tests, color deficiencies would have become manifest in the grossly unaffected eye as well as in that which showed such pronounced faults.

Speaking for the committee from the A. M. A. which submitted standards of vision for automobile drivers, Dr. Posey said that while it would have been very desirable to include tests for color-blindness, it was deemed impracticable to do so. The tests involved such a multitude and so many would have been disqualified by color-blindness, that it would have been impossible to have had standards rejecting the color-blind accepted by the Commonwealth.

## Pulsating Exophthalmos

Dr. William M. Sweet exhibited a man, aged thirty-four years, who received a blow on the left side of the head by some blunt instrument in the hands of a thief in November, 1924. He was removed to a hospital several hours later and was unconscious for twelve hours. There was bleeding from the left ear. Six weeks later the left eye began to gradually turn upward, without exophthalmos. Both eyes began to push forward nine weeks after injury, the protrusion being more marked on the left side. He was under treatment in a hospital from December 16 to March 22. The reports made during this period showed medical, neurological and nose and throat examinations negative; no fracture of the skull by the *x*-ray; blood and spinal Wassermann negative, and the eye-grounds of both eyes normal. No bruit was found by the hospital physician, nor did the patient notice any unusual noises in the head. While in the hospital two operations of excision of the edematous conjunctiva were performed. Photographs made at this time showed bilateral exophthalmos, the left eye probably slightly more prominent.

In May, 1925, six months after the injury, he first noticed "pumping" in the right eye, which has since continued. The exophthalmos of the left eye gradually subsided, the right eye remaining prominent.

In November, 1925, he was admitted to Jefferson Hospital. There was marked exophthalmos of the right eye, moderate of the left, with ectasia of the conjunctiva of both eyes, especially of the lower lids. The protrusion of the right eye increased with each heart beat. Exophthalmometer measurements showed: right eye, 28 to 30; left eye, 18. Rotation of right eye limited slightly above, below and outward, nearly abolished inward. Pupils: right eye, 3.5 mm.; left eye, 3 mm.; both react 1 mm. Right eye media clear, optic disk with preserved cupping; old inflammatory exudation surrounding margin, veins full and tortuous, arteries slightly smaller than normal. Left eye, no marked fundus changes although veins tortuous, but less than in right eye. Vision: right eye, 10/200; left eye, 20/40. All physical tests normal. The bruit clearly heard by the patient was noticed over the right eyeball, the brow and inner margin of the right orbit, and slightly beyond the median line. The patient found that by pressure at the inner angle

of the orbit he was able to abolish the bruit. Dr. Thomas A. Shallow saw the patient in consultation with a view of operative interference.

Discussion. Dr. Thomas A. Shallow said that this case presented two unusual features: First, exophthalmos appearing first in the left eye and shortly afterward in the right eye, so that within two weeks a double exophthalmos was present; and second, the late origin of the bruit. The first symptom of pulsating exophthalmos is usually bruit. In this case the bruit did not manifest itself for over four months after the accident and three months after the appearance of the exophthalmos. A bruit was noticed over the right eyeball and the right frontal sinus and a thrill at the inner margin of the right orbit. The bruit was distinctly audible to the patient. The thrill was transmitted toward the left part of the head somewhat beyond the median line. The patient is able to abolish the bruit by pressure on the inner aspect of the nose adjacent to the eye. Several months later the patient noticed that the left eye was not as prominent, and at the present time there is slight exophthalmos as compared with the right eye.

The patient was admitted to a hospital for treatment in December, 1924, one month after the accident. At that time the patient did not hear a bruit himself, and if a bruit had existed it certainly would have been found by the hospital physician. The patient underwent operation and a portion of the swollen conjunctiva was removed from each eye. There was still bilateral exophthalmos and the conjunctiva on each side was swollen. Photographs exhibited by Dr. Sweet leave no doubt that a bilateral exophthalmos did exist at that time. The first problem before any surgery was contemplated in this condition was to determine, if possible, the location of the arteriovenous fistula. An explanation of why the exophthalmos receded on the left side and then developed and persisted on the right side, might be helpful. Was the left-sided exophthalmos due to a hemorrhage behind the orbit? The history shows that the exophthalmos on the left side did not manifest itself for one month after the accident. If the exophthalmos had been due to hemorrhage its appearance would have been manifest very shortly. It could not have come on at the time when the hemorrhage, if it had existed, would have been practically absorbed. Did this patient

have an arteriovenous fistula on each side? If we consider this possible, then, in the absence of the thrill and bruit at the present time, a spontaneous cure of the arteriovenous fistula had occurred on the left side.

Dr. Shallow believed that the arteriovenous fistula was on the right side of the head and had been on that side only. The thrill and bruit being most manifest on the right side of the head over the frontal sinus points to the right side as the location. The recession of the left eye was probably due to the fact that the communication between the carotid artery and the cavernous sinus on the right side was in close relation to the origins of the circular sinus. A small tear in the carotid let blood flow into the right cavernous sinus directly opposite the origin of the circular sinus, so that at least a portion of the arterial bloodstream went directly across through the circular sinus into the ophthalmic vein of the left side. Later, either the carotid opening enlarged and all the blood then flowed into the right cavernous sinus or else a curative clot formed in the circular sinus or in the left ophthalmic vein. On account of the distance to the left side from the arteriovenous communication on the right side, the slow circulation of the venous blood, the left superior ophthalmic vein in all probability became thrombosed and a spontaneous cure was practically effected on the left side. With the thrombosing of the left ophthalmic vein the full force of the blood passed directly to the right ophthalmic vein, at which time the bruit probably manifested itself. He, therefore, recommended the ligation of the common carotid artery in the triangle of necessity and not ligation of the common carotid higher up or of the internal carotid. The principle of Halstead, who said that the nearer to the central organ of circulation the ligature is applied the greater the possibility of the establishment of collateral circulation, should be applied in this case.

## A Case of Tumor of the Orbit Wrongly Diagnosed as Sinus Disease

Dr. Wm. Campbell Posey exhibited a case of tumor of the orbit wrongly diagnosed for a time as disease of the sinuses, which occurred in a Jewess, aged nineteen years. The growth, the size of a horse-chestnut, had occupied the upper portion of the orbit and had given rise to quite marked exophthalmos. *X*-rays

of sinuses and orbit were negative, but a rhinologist had opened all the sinuses in the conviction that the orbital condition was secondary to a disease of these cavities. After several weeks of observation, operation was decided upon, and the tumor, a spindle-celled sarcoma, was removed by Dr. Posey without difficulty through an incision made just below the orbital ridge. Recovery was rapid and complete, only a faint scar remaining.

Dr. Posey said that twenty-five years ago ophthalmologists were busily engaged in calling attention to the frequency to which orbital affections are secondary to sinus involvement, today there is difficulty in persuading some rhinological colleagues that *all* orbital affections are not occasioned by disease of the sinuses. Many rhinologists are too loath to declare the sinuses free from involvement until they have opened and explored all, a dangerous and usually a totally unnecessary procedure. Ophthalmologists should be better acquainted with the anatomy of the orbit and should not hesitate to undertake surgical intervention on that cavity, always, however, when possible, with the aid of a rhinologist.

## Early Hays Knife-needles

Dr. Posey presented a set of Hays knife-needles which had formerly been in the possession of Dr. Isaac Hays. He called attention to the prominence of this surgeon, who died in 1879 at the age of eighty-three. He was best known, perhaps, as an author, having edited several works on diseases of the eye, the most notable being his edition of Lawrence's celebrated treatise on ophthalmic diseases. Dr. Posey said the Hays knife is still in use at the Wills' Hospital, although Knapp's and Ziegler's modifications of it are more commonly employed.

Dr. Posey also exhibited a note in Sir William Lawrence's handwriting on a bill from an ophthalmic instrument house in London, dated 1835, for instruments bought for his friend Dr. Hays.

Dr. Chance expressed his gratitude for the donation of Dr. Hays' instruments. He hopes that his may be the beginning of a useful collection of ophthalmological objects, to form the nucleus of an historical museum. The curator of the college museum has promised to provide a case for whatever instruments we might collect and

isolate the Section's deposit from the general collection, thereby to exhibit what might be of valuable interest to the ophthalmologist. Dr. Chance pleaded for further donations by the Fellows of their now abandoned instruments and other objects to be shown as milestones in the history of the development of ophthalmological science and practice. One of the most valuable contributions to the success of the recent ophthalmological congress in London was the truly brilliant collection of instruments and data displayed in the museum section. The Fellows of this College have themselves been foremost in America in ophthalmology and their private belongings ought certainly to be preserved for future generations.

# PROCEEDINGS

OF THE

# SECTION ON OTOLOGY AND LARYNGOLOGY

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JANUARY 21

## Some Observations on Certain Forms of Chronic Sinusitis

BY ROSS HALL SKILLERN, M.D.

In using the term chronic as applied to diseases of the accessory sinuses of the nose, to just what condition do we refer? Is it to one that has continued for a long period of time with little change as to its symptomatology and with no especial reference to its ultimate termination, or is it to a condition that implies a permanent pathological change with little hope of spontaneous recovery regardless of the length of time the inflammatory process has continued?

The word chronic takes its derivation from the Greek word χρόνος, meaning time. We would then infer from this that our first interrogation were correct, and that when speaking of a chronic sinusitis the viewpoint of length of time was implied rather than reference to the actual pathological condition of the sinus mucosa.

You will immediately say: "True; but one condition presupposes the other: When an infective process continues for a certain length of time in an accessory sinus, the mucosa reacts in such a manner as to permanently change its character. In other words, the passage of time and permanent pathological changes in the mucous membrane are synonymous."

Well, now, are they? Does the presence of certain symptoms of a chronic nature always mean that the infection must of necessity been continuing over a given period of time? Most assuredly not. Paradoxical as it may seem, the infection may start as a chronic

disease, as, for instance, in maxillary empyema of dental origin, where the continued slight infection from the minute fistula in the carious tooth slowly and gradually spreads out into the floor of the antrum until finally the entire cavity is involved. The process from its very inception has been essentially of a slow and chronic nature, at least as far as the symptoms were concerned. On the other hand, our usual conception of a chronic stage is the condition of comparative quiet that follows after the acute symptoms have run their course. Now nobody can fix a time-limit on which this occurs; no given length of time can be arbitrarily stated in which an acute disease will become chronic. It depends entirely upon the numerous causes and combinations of causes which have given origin to the disease, together with the favorable or unfavorable anatomic configurations, not to mention the virulence of the attacking microörganisms or the susceptibility of the individual. There exists no sharp line of deviation either clinically or pathologically between the acute and chronic stadia. Even in autopsy findings it is difficult to determine whether the diseased sinus has been acutely or chronically affected.

The cause of the chronicity depends upon many factors which I give in the order of greatest importance.

Interference with normal aëration and drainage. This must be divided into natural and acquired:

1. *Natural.* *a.* In this category belong the anatomical peculiarities, such as a deviated nasal septum, particularly high up, causing the nasal passage to be extremely narrow on that side and wedging the middle turbinate against the bulla and lateral wall of the nose.

*b.* A long and narrow nasofrontal duct, which would become occluded at the slightest swelling of the lining mucosa, thus closing the frontal sinus like a cork in the neck of a bottle.

*c.* Deep recesses and partial septa in the sinus cavities, predisposing to the retention and stagnation of contained secretions.

*d.* Large, rolled-out, middle turbinates hugging close to the lateral nasal wall, thereby occluding the normal drainage passages.

*e.* In the case of the maxillary sinus: Roots of teeth extending into the floor of the antrum.

2. *Acquired.* *a.* Repeated attacks of coryza, causing a chronic thickening of the mucosa with gradual interference to drainage and ventilation.

*b*. Inflammatory changes in the sinus mucosa, causing an inhibition to the movement of the cilia, thus preventing them from ridding the sinus cavity of the invading microörganisms.

*c*. Type of infecting organism. No matter what the type of the primary infecting germ may have been, after a certain length of time one of the commoner varieties, either the staphylococcus aureus or the streptococcus, not usually the viridans or hemolyticus, is the predominating organism. In my experience, if the streptococcus is mostly present the disease runs a rapid course, while, conversely, if the staphylococcus is predominant the course is apt to be slower and much less violent both in its subjective and objective symptoms. I recall particularly a young man coming into the hospital after a peculiarly severe attack of acute frontal sinusitis from deep diving. He presented himself for diagnostic purposes, feeling much improved over his condition of the previous week and rather resented the idea of an operative procedure. But at the time of operation at least half of the frontal lobe was covered by an extradural abscess. The culture showed a pure strain of staphylococcus aureus.

So much, then, as a preface to the consideration of the actual conditions in the various sinuses.

We propose, with your toleration, to treat only with the chronic affections of the true sinuses, namely, the frontal, maxillary and sphenoid, or those which are surrounded by hard, unyielding bony walls and situated outside of the general nasal cavities. The ethmoid capsule is a totally different structure whose chronic pathology is a chapter unto itself, the consideration of which at this time would be too great an indulgence upon your already overtaxed patience.

The true sinuses, although reacting in a similar manner to chronic infection, nevertheless exhibit quite a different symptomatology, due to their anatomical configuration, differences in drainage mechanism and position. Thus, in certain ones, the formation of a mucocele is comparatively common, while in others seldom seen; again, rupture and fistula-formation is often noted with, for example, chronic frontal sinusitis and almost never in any of the others.

Let us now consider some of the commoner manifestations of chronic infection in the individual sinuses.

*The Frontal Sinus.* The ordinary case of chronic frontal sinusitis usually results from repeated attacks of so-called cold in the head,

which may or may not have been traced to an earlier attack of influenza. The patient states: "Doctor, whenever I take cold my old sinus trouble gets worse." It can very well be compared with a chronic appendix. The patients are really only uncomfortable during the exacerbation of the attacks. The pathological changes in the mucosa in these cases are slight and, if given half a chance, would quickly heal and probably never more bother the patient. The astute sinuologist after a preliminary examination recognizes this and looks for the causative factor of the chronicity, knowing well that if this is removed regeneration will immediately commence in the inflamed sinus mucosa with an ultimate return to normal. In other words, the deflected septum, cystic middle turbinate or what not that was of just sufficient obstruction to carry along a low-grade form of chronic inflammation in the sinus, if corrected, removes that factor which prevented a spontaneous cure after the original acute attack following influenza.

Under these circumstances it is far better to seek out these obstructions to aëration and drainage and remove them, than to employ our time trying to lavage the sinus with all sorts of old and new antiseptics and expect a result that will last much longer than the patient's visits.

Suppose, however, that for reasons beyond our control we are too late with the intranasal surgery, or that it had already been done when the patient came into our hands, and well done at that, yet for one reason or another the progress of the disease had remained unchecked. It seems to me that this is the type of frontal-sinus case that usually comes to us, tired of the periodical suffering and willing to submit to any procedure which in our judgment will give permanent relief. It is these very cases, I am sorry to say, that hitherto have been considered as indicated recipients for some form of the external operation. How many times have I done an external radical on these sufferers which may have brought freedom from their pain, but, as I see it now, could have been just as thoroughly and perhaps quickly relieved by some less extensive resection of bone and cutting of tissue. I freely admit in my own practice that I have to all intents and purposes eliminated the external method as originally advocated by Killian. I have long since seen the futility of extensive resection of bone in the class of cases just mentioned and have guided my hand accordingly, and furthermore, have procured just as good, if not better, results than I had

hitherto obtained. When the discharge has become foul-smelling the prognosis for a favorable outcome becomes inversely as to the fetidity of the secretion, and greater aëration and possibly the curette become indicated; but even though good results follow the extensive procedures, I do not in the main, gentlemen, subscribe to the old adage that "the end justified the means," when lesser means would have sufficed to bring about equally as good if not happier results.

When rupture externally, with fistula formation, occurs, the entire situation instantly changes. Any intranasal procedure, however extensive, is no longer considered, as it does not offer any possibility of a cure. An external operation, of unlimited extent if necessary, is indicated in order to bring all diseased parts under immediate inspection; but even here it is seldom desirable to resect the great amount of bone as was advocated by Killian. Fistulas will heal under proper drainage, and sufficient drainage can be installed without completely skeletonizing the entire sinus.

Another variety, or rather an end-result, of chronic inflammation is the formation of a mucocele or cholesteatomatous mass. In operating, a mucocele being present, the choice of operation is not with the surgeon, but he must shape his ends according to the size and extent of the cele. Cholesteatoma of the frontal sinus I have never seen; but, judging from the habits of our otologic brethren, a radical operation as extensive as necessary would also here appear to be indicated.

*The Maxillary Sinus.* Chronic inflammation of the maxillary sinus presents a wide range and variety of symptoms and indeed some aspects which are not to be found with any of the other sinuses.

Perhaps the mildest form of chronic infection of the antrum is that one seldom referred to and never described. I mean, pathologically speaking, when the antral mucosa has to a greater or lesser extent undergone polypoid changes, but gives rise to no particular subjective symptoms. Needle-puncture elicits but a thick, clear straw-colored fluid which internally mixes with the injected solution and scarcely changes its appearance. As a matter of fact, this condition is seldom diagnosed except by accidental or intentional needle-puncture. The significance of this infection is not in itself, but rather in what it may cause or terminate into. An antrum in this condition sooner or later becomes infected with the common microörganisms of suppuration, and then we have a chronic puru-

lent sinusitis which, owing to the long-continuing, permanent, pathological changes in the mucous membrane, defies any counteraction of ours to allay the inflammation short of the chisel and curette. Occasionally, it is true, after a number of lavages, the secretion loses its purulent characteristics and returns to a clear, straw-colored consistency; but, sooner or later, infection becomes so widepsread and acute attacks so frequent as to make the patient's existence so miserable that he demands complete and permanent relief.

The proposition often arises in these cases, how long shall we continue the needle-puncture and lavage before recommending operative procedures. That is a question which will continue as long as we have conservatives and radicals. The first (conservatives) are overly sanguine, the latter unduly impatient. The former will contend that cures have been reported only after fifty or more needlings with lavage. The latter will retort that many cases, through ill-advised procrastination, have been obliged to undergo an external radical operation to insure a successful outcome when a simple intranasal procedure would have sufficed if done at an earlier stage of the disease.

That brings us to the value of antiseptics to use as irrigating menstrua. I must confess to disillusionment and shattered hopes, particularly since the War. Since that period I used the various chlorine solutions with the greatest of anticipations, only in the end to experience disappointment; then followed acroflavine, mercurochrome and now dibromin: The first two being thrown in the discard and the last is in a fair way to follow. I have but three menstrua that I now regularly use: Normal saline solution, alcohol and nitrate of silver in varying strengths. The latter is but a last-resort method before turning to the knife, and occasionally, but only occasionally, does it make good. The character of the secretion, to my mind, is one of the most reliable indications as to the state of the antral mucosa—again pathologically speaking. A thick, heavy mass or masses of yellow pus, which show a tendency to coalesce, indicates that the lining membrane still possesses plenty of working cilia and, *ipso facto*, cannot be profoundly diseased, at least in any appreciable area. While, on the other hand, a thin, whitish, fetid discharge, which freely mixes with the injected fluid to form a milky, granular mass, shows only too clearly that the cilia are not only nonfunctionating, but gone, and metamorphosis into the squamous type is already far advanced.

Now, while on this subject, a word regarding the danger of the needle-puncture. While comparatively little has been written apropos of this, nevertheless, the few articles that have appeared have apparently made a deep impression and attracted widespread attention. To my mind the danger has been exaggerated beyond all degree of its relative importance. I have never yet seen an instance in which needle-puncture was done (properly or improperly) that was even followed by alarming symptoms. This includes numerous cases of air injected into the orbital cavity and the preantral region, and in one case where a quantity of solution was injected into the tissues around the eye. However, in making this puncture and lavage, several technical points are strictly adhered to:

1. The puncture is always done through the inferior meatus.
2. A small quantity of air is always injected under the slightest possible pressure.
3. If resistance is felt, the pressure is removed and a stylet passed through the needle.

It would appear, in most of the fatalities that came to autopsy, that portion of the antral mucosa lying around the point of entrance of the needle was detached from the underlying bone, showing that the injection either of air or fluid was directly responsible for the sudden death. If the three postulates just referred to were followed in introducing the needle, perhaps the occurrence of these fatalities would be greatly mitigated or even entirely overcome.

Another form of chronic maxillary sinusitis is that resulting from a decayed tooth, the infection spreading through the root canal and out the foramen at the extreme tip of the root. The occurrence, compared to the sinusitis of nasal origin, is comparatively rare, at least in my experience, although it is curious to note the wide divergence of opinion of different observers, the scale running from 5 to 100 per cent; I was inclined to accept about 20 per cent as the proper proportion, but, in reviewing the cases that have come under my observation to date, it would seem that even this figure is now too high. This form of the disease, due probably to its insidious chronicity, is very prone to become infected with the ordinary saphrophytic organisms connected with putrefaction and become very fetid.

Still another form of chronic antral disease is the formation within the sinus of a solid mass resembling cream-cheese. This

may be due to the infecting germ for some reason becoming attenuated, and the secretion, being unable to escape, gradually loses its fluid content, the residue forming this cheesy material.

Another, but perhaps less frequent cause, is due to the occlusion of the mouth of one or more mucoid glands, which results in a mucocele, the contents of which later become solidified. A moderately large opening beneath the inferior turbinate, through which in succeeding treatments it was possible to wash out this caseous substance, has sufficed for me in the few cases that I have been called upon to treat.

*The Sphenoid Sinus.* Probably less is known about the chronic conditions in this cavity than in any of the others, on account of the fact that it has been less under direct observation for reasons that are obvious to all. I know of no condition more difficult to diagnose than a low-grade, chronic, nonsuppurating sphenoiditis that at best has given rise to but vague symptoms referable to the head. But we are getting too far afield. To return to our subject, chronic inflammation of the sphenoid mucosa may extend all the way from a low-grade, almost nonsecreting and symptomless catarrh to a profuse purulent discharge with all sorts of pains and aches in, near and remote portions of the body.

Included in this low-grade form, but in a more advanced stage than that mentioned above, is the hyperplastic type of sphenoiditis. The most prominent symptoms of this does not lie in the nose, but outside of it, in the form of vague but intractable occipital headaches, often associated with occular disturbances and a postnasal discharge which, on examination with the nasopharyngoscope, usually reveals nothing.

The chronic purulent form is much franker in its manifestations, but, as they are so well known to you, I will merely refer to them in passing. One symptom, however, that I have noted in several cases but have never heard described, is a dull pain in the supraorbital region of the affected side. On opening the sinus this invariably disappeared.

With this, gentlemen, I will close. While I appreciate that this presentation has been sketchy and rambling, nevertheless, it seemed to me to be more suitable for a gathering of this sort than the usual textbook representations that odinarily hold sway. If I am correct in this assumption my time has been well spent; if not, I trust you will take the will for the deed and bear with me accordingly.

# Perforation of the Faucial Pillars, with Report of a Case

BY EDWARD H. CAMPBELL, M.D.
(By Invitation)

(From the Department of Otology of the University of Pennsylvania)

There recently came to my attention, in the ear clinic of the University of Pennsylvania hospital, a patient with a perforation of the right anterior faucial pillar. Cases of this kind although not extremely rare have been but infrequently placed on record, and I have taken the opportunity that this case affords of reviewing and summarizing the literature on the subject, using as a text the following report of my own case.

M. B., a white girl, aged nine years, has a history of considerable illness, consisting of granulation of the eyelids, pneumonia and mastoiditis at one year of age, eczema of the scalp and face a short time later, chicken-pox at six years of age and a severe condition of the throat at the age of two. The exact diagnosis of this throat condition is greatly in doubt. The mother states that the child's throat was very sore on the right side for three months, but that the patient was not confined to bed, although she had frequent convulsions. Apparently no operations were performed; but, according to the mother, the sore-throat seemed to "eat the tonsils away." After that the patient had no further trouble with the throat, but at the age of three the left ear started to discharge pus and has continued to do so ever since. She has been treated for five months for eczema of the face and scalp, with considerable improvement. A negative blood Wassermann was obtained three months ago. The patient has two younger brothers and one sister all healthy and apparently normal. There is no history of abnormalities in either parent.

Physical examination shows a well-developed girl of poor color and with an eczema of the face and scalp. Her eyes are the seat of a marked strabismus. The left ear shows a thick, foul purulent discharge, but her hearing is only slightly impaired. Her throat presents small and somewhat embedded tonsils, the right one being closely adherent to both anterior and posterior pillars. Through the right anterior pillar, about opposite the middle of the tonsil, there is a narrow, oval perforation about 1 cm. long and 2 mm. wide with sharp smooth edges. The rest of the physical examination is negative.

Etiology. The etiology of perforations of the faucial pillars and of the soft palate has been the subject of considerable discussion and decided difference of opinion.

McKenzie,[1] of London, in discussing their origin, says: "Perforations of the anterior pillars of the fauces are often bilaterally symmetrical, and this feature, combined with an absence of scarring, has led to the belief that they must be of congenital origin. As against that view, there is the undoubted fact that Sir Robert Woods and other reliable observers have seen them in process of formation in severe scarlatina. That this is probably the origin of all such peforations is supported by the circumstance that they have not, so far, been reported as occurring in young infants, and that the patients have or have had enlarged tonsils, the swelling of which during the attack causes the perforation by pressure atrophy." He also says that perforation of the palate, hard or soft, is a syphilitic manifestation.

Tilley[2] says: "There can be little doubt that sometimes perforations of the anterior pillars are congenital in origin and they may be associated with bifid uvula and other local evidences of maldevelopment. In other instances such perforations may result from ulcerative lesions occurring in the course of scarlet fever. Finally there are perforations of the fauces due to the lesions of tertiary syphilis." The literature on anomalies of the soft palate shows that only 33 cases of perforation have been reported, including both the anterior and the posterior pillars.

Posterior Pillar. Those of the posterior pillars are very rare, only 7 having been recorded up to the present time. The first of these was reported by Schmiegelow.[3] His case showed a perforation in the right posterior pillar, oval in form, 1 cm. in length and 4 mm. in width. The borders of the opening were sharply defined and there was no evidence of cicatrization.

Jurasz,[4] in 1891, recorded the second case, a perforation in the upper part of the left posterior pillar with no trace of cicatricial tissue. He also presented a case of perforation of the right anterior pillar.

In the next year, Hajek[5] reported 2 more cases. One showed bilateral symmetrical perforations in the posterior pillars; the other case presented a double opening in the same posterior pillar, the upper one being round and the lower one in the form of a fissure. Hajek also is credited with a report of 2 cases of perforation of the anterior pillar.

Rethi,[6] in 1893, reported a case of perforation in the left posterior pillar. This one also showed a smooth, regular border with absence of any scarring.

Raoult and Finck[7] presented, in 1898, a case of bilateral elongated perforation of the posterior pillars. The openings were symmetrically placed and this was largely their reason for putting the case in the class of congenital anomalies.

Collett and Troullieur[8] noted, in 1905, in a man, aged eighty-two years, two perforations of the left posterior pillar and one perforation of the right. These openings were smooth and regular, with long axis running parallel with the muscular fibers. There were no signs of scarring and the patient could remember no sore-throat at any time. These authors considered the condition as one of congenital origin.

Anterior Pillar. Perforations of the anterior pillars are more frequent than those of the posterior. In the majority of instances they are bilateral and symmetrical, and almost always are found to be free from adhesions or contractions. They usually are untraceable to either congenital or acquired syphilis, but are considered by most authors to be congenital deformities.

One of the first cases on record was reported by J. Solis-Cohen.[9] He reported such a case in 1878, the examination of the patient showing an elongated oval aperture in the anterior pillar of each side just above the lingual attachment. The rest of the throat was free from any signs of disease. He says that an occasional anomalous condition of the palate consists in a separate mucous investment of the palato-glossus muscle in the anterior fold of the palate,thus leaving an opening which might be mistaken for ulcerative destruction of the palatal tissue. In the same article Cohen referred to a somewhat similar case reported by Wolters, in 1859, which appeared to be the only other one on record at that time. In Wolters's case the anterior pillar of each side was split, a cord stretching obliquely downward and slightly outward from the uvula to the side of the root of the tongue. There were no traces of cicatrization.

The next case, reported by Lefferts,[10] was of a girl aged nineteen years, who had a perforation the size of a small pea through each side of the velum palati. The edges of the openings were smooth and rounded and free from cicatrical tissue. The patient had never had any severe affection of the throat and remembered that the openings had always existed. Lefferts considered the case one of congenital origin due to arrest of development.

Chiari[11] recorded a case showing an oval perforation in each

anterior pillar, with smooth borders and no traces of cicatrization. The perforation on the right was larger than the one on the left. His case had a history of throat trouble at one time which might have been ulcerative in nature. He concluded, however, that it was due to arrest of development.

Claiborne[12] reported, in 1885, a case with a hiatus in the anterior pillar of the right side with congenital absence of both tonsils. The hiatus was not complete, but consisted of a furrow with edges not sharply defined and no signs of cicatricial tissue. There was no history of previous throat trouble.

Schapringer[13] was apparently the next man to report a similar case. His also was a one-sided perforation of the anterior pillar, with a rudiment of the left tonsil and absence of the right. His case had had a severe attack of diphtheria in early life, but he was inclined to believe the anomaly congenital in nature.

Fowler[14] recorded bilateral symmetrical perforations of the anterior pillars in 1889. These openings were unusually large and the tonsils were reduced to mere stumps, from which grew right across the base of the tongue a broad and elevated ridge of tonsillar tissue (the lingual tonsil?). The patient had had a severe phlegmonous tonsillitis during an attack of scarlet fever some years previously. Fowler considered perforations of the anterior pillar as always acquired. He thought that if careful examinations were made of the margins of the openings cicatricial tissue would be found, showing them to be due to ulceration. In all the cases he had observed he had obtained a history of scarlet fever or recurrent attacks of quinsy, and this led him to look upon all these perforations as caused by suppurative or phlegmonous inflammation in the tonsils. He even goes so far as to say that the lesion is most probably a sign of antecedent scarlet fever.

Toeplitz,[15] in 1892, described a case with an opening in each anterior pillar, symmetrically placed, the right one slightly larger than the left. He considered them to be of congenital origin.

In the next year, Broeckaert[16] reported a case with symmetrical openings in the anterior pillars, oval in form, with no evidence of scarring and with only remnants of tonsils. He placed the case in the class of anomalies due to arrest of development.

Morrice[17] cited 4 cases of perforation of the anterior pillars: 1 of these followed scarlet fever and 3 gave a history of diphtheria.

Seifert[18] reported an elongated perforation of the upper part of

the left anterior pillar, with rounded borders and no evidence of cicatrical tissue.

Meijes,[19] in 1894, presented a case having an elongated oval perforation of the right anterior pillar with no signs of cicatricial tissue and with a negative previous medical history. He thought the condition due to arrest of development.

Garel,[20] in 1894, reported a case of bilateral perforation of the anterior pillars and a case of unilateral perforation, without evidence of any scarring. He considered these openings due to faults in development.

Three years later, Griner[21] recorded a case of a man, aged twenty-two years, with a large perforation of the left anterior pillar. This opening extended from a level of the base of the uvula to the lower extremity of the pillar, a distance of about 3½ cm. The patient gave a history of trouble with the throat at an early age. Histological examination of a section of the border of the perforation showed the presence of cicatricial tissue, so the lesion was not considered to be of congenital origin.

Ehrmann,[22] in 1902, presented a patient with a circular opening 8 mm. in diameter in the soft palate. He considered the lesion congenital.

Grant,[23] in 1910, reported a perforation of the soft palate, in a girl, aged sixteen years. The opening was situated above and to the right side of the base of the uvula. The nature of it was undecided. In its neighborhood there was no such cicatricial tissue as would accompany a specific perforation, but there was a history of such traumatism as could have accounted for it, namely, an operation on the tonsils in early childhood.

Bumba,[24] twelve years later, presented a patient, aged thirty-two years, with symmetrical openings in the anterior pillars, the right one somewhat larger than the left and both situated opposite the superior extremity of the tonsil. The edges of the perforations were sharp and the surrounding tissue normal in appearance. The tonsils were of normal size and the patient gave a negative Wassermann reaction. The lesion was considered to be of congenital origin.

Rouget,[25] in 1923, reported a case of multiple perforations of the anterior pillars. There was one opening in the right pillar 15 mm. long and 5 mm. wide, and two smaller ones in the left pillar, one above the other and separated by 1 cm. of apparently normal

tissue. These perforations had a punched-out appearance and beneath them were somewhat hypertrophied tonsils. There was no history of personal or hereditary syphilis and the Wasserman was negative.

In the same year, Trinder[26] recorded a case of perforation of the soft palate with double uvula. The perforation, 1 cm. long and ½ cm. wide, was situated in the center of the soft palate. The uvulæ were of normal size, symmetrically placed, lateral to the median line. From the history, the patient apparently had had the condition since birth. Trinder relieved the condition by grafting one of the uvulæ over the perforation, thereby removing one uvula and closing the opening in the soft palate.

Nearly all the authors quoted have speculated on the cause of these conditions. Most of them believe the perforations to be of congenital origin. Nearly all of the cases reported have been in adults, and in these patients we are dependent upon their often unreliable memory for the previous medical history of the case. If there had been a few cases reported as having been observed in early infancy, before any catarrhal or ulcerative condition of the throat could have occurred, it would tend to prove more decisively the congenital nature of these perforations.

In the case I have reported, although the perforation has sharp, smooth edges with no cicatricial tissue in its neighborhood, the previous medical history leads me to believe it to be of inflammatory rather than of congenital origin. The tonsil beneath this opening is small, embedded, closely bound to the pillars by adhesions and with every appearance of having been actively diseased. It seems very possible that the condition could have been caused by the persistent inflammation of the right side of the throat which the child had had seven years ago.

Conclusion. In this paper I have endeavored to collect all the recorded perforations of the faucial pillars that have appeared in medical literature, I realize that this presentation offers nothing to alleviate the many ailments to which humans are subject, but I hope that it is justified if only as a possible collective source of reference to conditions of this kind.

I wish to extend many thanks to Dr. Fetterolf, whose aid and guidance were invaluable in preparing this paper, and to the members of this Section for the privilege of presenting it to them.

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## Observation on the Use of the Artificial Drum Membrane

BY WILLIAM A. HITSCHLER, M.D.

History. A brief review of some, but not all, of the literature discloses the fact that an artificial drum membrane was referred to by Marcus Banzer in the year 1640, and by Itard, Deleau, Tod and Lincke from 1815 to 1845. The next references were in 1848 and 1849, by Yearsly and Erhard, respectively—although it was Toynbee who first attracted the attention of otologists to this subject by his own invention in 1852. Other forms of this artificial aid to hearing were contrived by Politzer, Lucae and others.

According to Politzer, it appears that "the invention of the artificial drum membrane was based upon the observations of aural patients who noticed a striking improvement in hearing when they touched the remnant of the membrane while trying to remove secretion from deeper parts by means of a rolled piece of paper or pencil."

*Type of Cases.* It is evident that an artificial device is indicated chiefly in cases where there has been partial or complete destruction of the drumhead with or without loss of one or more ossicles. It is true that there are cases in which complete destruction of these integral parts has left the hearing power practically unimpaired, but they are rare. I can recall one such case in which the hearing power for the whispered voice was thirty feet. But any loss of substance of the drumhead, or drumhead and ossicles, is usually accompanied by more or less deafness, and the degree of deafness is, roughly speaking, in direct ratio to the amount of destruction, particularly if the destruction be in the region of the oval window. It may be well to note that in the three most successful cases that have come under my observation the destruction was practically complete, and also, in those cases where portions of the malleus and incus still remained *in situ*, the artificial drumhead was of distinctly less service. But it may not be wise to draw any conclusions.

The success attendant upon the use of the artificial drum membrane, if so it may be called (for it does not function like the real membrana tympani in the sense that it vibrates), has been so far from gratifying in my hands in the vast majority of cases that it has aroused no great measure of enthusiasm. The only reason I have for referring to the subject is the brilliant success resulting in 2 patients who were transformed from a silent to a hearing world, and the reasonably good result in the third. In 1 patient it probably forstalled a condition of melancholic despair. Other patients, in whom results seemed fairly promising, became discouraged at the prospect of oft-repeat visits and gradually drifted away.

*Varieties of Artificial Membrana Tympani.* These artificial devices are of various kinds. Illustrations of Toynbee's, Politzer's and others, with their modifications, have adorned the pages of textbooks for many years and need no description. In cases of simple perforation, involving a small portion of the membrana tympani, pieces of court plaster, writing paper and the like have been employed with more or less success; in my hands with less. These do not remain long *in situ*, but are forced into the external auditory meatus by the growing epithelium. In some cases the closure of a small perforation has resulted in increased deafness.

Yearsly and Erhard used a cotton ball about the size of a small pea. It proved extraordinarily successful in 1 of my cases, but in other cases was not as efficient as the cotton disk.

The disk is made of absorbent cotton and is cut to resemble roughly the size and shape of the normal drumhead. When moistened it is about 1 mm. thick. The thickness is an important factor. A disk either too thin or too thick is of scant service. Sterilized white silk (white to lessen the color contrast with the skin of the meatus), with loose strands just long enough to reach to the concha, is tied to the posterior inferior margin of the disk to facilitate removal by the patient.

*The Moistening Solution.* While Politzer states that a ball of *dry* cotton may be used, and has given better results in some cases, it has been my experience with the ball and the disk that moistened cotton is superior. Various media may be employed, *e. g.*, normal salt or boric acid solution, alcohol of various percentages, liquid petrolatum, glycerin, etc. Of these, glycerin has proven the most serviceable; 5 to 8 per cent carbolic acid may be added to satisfy antiseptic requirements.

The degree of moisture is another factor and an elusive one: Somewhat less than the full capacity of the cotton to absorb has yielded the best results; but it is a matter of experiment. Should the disk become dry while in position, the patient usually notes a decrease in the hearing power. A little moistening restores its efficiency.

*Technic.* The disk is applied in fairly intimate contact with the internal wall of the middle ear, especially in the region of the oval window, which is apparently the responsive area. This may require a little time and some patience. Proper contact is essential, for the slightest deviation from the correct position usually manifests itself in decreased hearing power. This may happen during instrumental manipulation of the disk, by an unintentional tug on the silken strands or by a forcible blowing of the nose. The patient usually notes instantaneously the moment of efficient contact.

When first applied, the artificial drum membrane acts as a foreign body and tends to produce inflammation and discharge. For this reason most authorities advise leaving it *in situ* but a few hours, to be reinserted in a day or two. Whatever other advantages this method possesses, it may not prove practical. The middle ear must establish a tolerance, and the sooner this is accomplished the sooner will the practical value of the device be appreciated by the patient. The disk may, therefore, remain *in situ* until inflammation is established, the patient being seen daily if necessary. Once

inflammation occurs, the disk is removed and the ear treated in the usual manner. When reactionary phenomena subside, a fresh disk is inserted, and this process is repeated until tolerance is established. This may require months, perhaps a year or two, but the inflammatory reaction becomes progressively less frequent and less severe and eventually ceases altogether. At least it ceased altogether in the 3 successful cases cited. Moreover, the lining of the tympanic cavity seemed to lose the characteristic behavior of mucous membrane and assume more and more the indolence and indifference of the scar tissue.

One can readily understand that this is a tedious method for relieving deafness, and unless the benefit be material few patients would care to continue. The successful cases, however, are decidedly enthusiastic.

When tolerance has been once established there is no further discharge and the period of time which the disk may be allowed to remain in the ear depends solely upon the degree of service rendered. In 1 case seven months elapsed before the disk was removed, and then but to observe the proprieties. With this particular patient the disk is removed only when the hearing power becomes insufficient for ordinary needs, otherwise it is left severely alone. In another case the best results were obtained by changing the disk once a week, and in a third case once daily.

The patient is taught to introduce the cotton himself. For this purpose a miniature and delicate dressing forceps, without serrations at the tip, is useful, likewise the Hassenstein forceps, but with the shank longer than in the original model. Very soon the patient becomes adept and often rivals and even excels the skill of the otologist. Occasionally, after having been left in position for a time, the disk becomes firmly adherent to the inner tympanic wall; moistening with hydrogen peroxide suffices to loosen it.

Politzer states that an artificial drum membrane is contraindicated "if it again sets up a discharge after an exhausted middle-ear suppuration." But there is a difference between the rekindling of a dormant, sinister suppurative process and the creation of one that is new and innocuous. However, we can cordially agree with Politzer that it is contraindicated if it increase a suppuration already existent; and we may go even one step further and say it is contraindicated as long as suppuration or inflammation of any kind is present.

*Altitude.* It may be interesting to note that in 2 of 3 cases alluded to the hearing was improved in the higher altitudes. One case reported that in Denver or any similar altitude he not only heard better, but that he was enabled to dispense with the cotton ball altogether. I have no explanation to offer for this phenomenon. He eventually secured a position in Denver and thenceforth his deafness was no longer a matter of concern.

Simple tuning-fork tests showed the usual reactions of obstructive deafness. The only particular change noted after the insertion of the artificial drum membrane was a greater appreciation of the higher tones of the Galton whistle.

*Results.* In the London *Lancet,* 1922, Dundas-Grant reports considerable success with the disk, but in the greater proportion of my cases the results have been disappointing. Many showed no improvement whatever, some a moderate improvement, and in only a very few could the improvement be called worth while.

In 1 case in which inspection showed no vestige of membrane or ossicles the hearing distance for the whispered voice without the cotton disk was from zero to 6 inches; with the disk, from 6 inches to over 23 feet, the average being around 10 feet.

In the second case inspection showed a mere rim of drum membrane in the anterior superior quadrant, the short process of the hammer and the head of the stirrup. Without the disk, zero to 2 inches; with the disk, 2 inches to over 23 feet, the average being around 15 feet.

My notes on the third case have been mislaid, and I quote from memory: Inspection showed no remains of either drumhead or ossicle; but the improvement here was most marked. Without the cotton ball the whispered voice was scarcely audible, while with it the patient heard nearly all words at 23 feet and over.

The livelihood of 2 of these cases depended upon their hearing power. With the third the question of livelihood did not enter. She was a young woman with a fairly comfortable income, but with an artistic and high-strung temperament which craved its fullest expression in the social contact which was fast being denied her by her affliction. Moreover, her health was being affected. To her the cotton disk was an open *sesame* to both social and physical comfort.

*Modus Operandi.* There have been a number of theories to explain the *modus operandi* of the artificial drum membrane; but, inasmuch

as the theory advanced by one authority is usually refuted by another authority, a review of this phase of the subject is rather amusing than enlightening. That it is based upon laws of physics is evident enough, and it may be well, perhaps, to leave the explaining to the physicists.

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## Thymic Death in an Adult During Local Tonsillectomy

BY DAVID N. HUSIK, M.D.

Death during a tonsil operation in an adult, due to a large thymus, is an exceedingly rare occurrence, and I wish to add this case to the large list of fatal cases during or secondary to tonsillar operations that have already been reported.

The thymus gland is a temporary organ belonging to the ductless gland system, as a rule attaining its full size at the end of its second year, when it ceases to grow and gradually dwindles, until at puberty it has almost disappeared. If examined when its growth is most active it will be found to consist of two lateral lobes placed in close contact along the midline, situated partly in the superior mediastinum, partly in the neck and extending from the fourth costal cartilage upward as high as the lower border of the thyroid gland. It is covered by the sternum and by the origins of the sternohyoid and sternothyroid muscles. Below it rests upon the pericardium, being separated from the arch of the aorta and the great vessels by a layer of fascia. The thymus is formed from two lobes, which often differ in size but are usually united so as to form a single mass. It is pinkish in color and its surfaces are lobulated. It is about 2 inches in length and $1\frac{1}{2}$ inches in breadth.

Status thymicus, or status lymphaticus, is a condition of bodily debility which is characterized by hyperplasia of the thymus and of the lymphoid tissues throughout the body, and also, especially in adult cases, by hyperplasia of the heart and of the arterial system. It is accompanied by a great lowering of the patient's power of resistance and believed to account for a large number of otherwise unexplained cases of sudden deaths.

About eight years ago I was called to explain the sudden death of a child, aged four years, two hours after a very simple tonsillectomy, with practically no bleeding, which was performed by one of our staff. The child was apparently well and out of the anesthetic, but she suddenly became blue and before the interne was called died. Not knowing any other cause for such a sudden death, she was signed as one of status lymphaticus.

It is a very old and oft-repeated observation that enlargement of the thymus is often the chief discoverable lesion in cases of sudden death from apparently insufficient causes. With regard to this coincidence there can be no doubt; but its explanation is obscure and has given rise to great differences of opinion.

Older writers on this subject believed that a large thymus caused death by setting up a fatal laryngismus, which they designated as thymic asthma. The laryngismus in these cases is only a symptom of a general nervous irritability and has probably nothing to do with the enlarged thymus. The mechanical pressure of the hypertrophied thymus on the trachea or bronchi or even on the lungs has been thought by many clinicians to play an important part in the causation of thymic death. To some it has seemed that the fatal syncope may be induced by direct pressure on the large vessels. Others have believed that it was due to pressure on the nerves—vagus, recurrent laryngeal, phrenic or sympathetic.

Arnold Paltauf has brought forward a new hypothesis which has met with more favor. In his opinion it was not proven that thymic death was due to pressure of the enlarged thymus on the trachea, bloodvessels or nerves; but he attributes thymic death to the patient having a peculiar lymphatico-chlorotic constitution, which he called status lymphaticus. This dyscrasia he describes as being characterized by a general enlargement of all the lymphoid tissues of the body, the enlarged thymus being merely one of its manifestations. The constitutional weakness was, in his opinion, sufficient to account for the fatal syncope as well as for all other symptoms.

The cause of status lymphaticus is quite unknown. It has been pointed out that in early childhood most of the patients are rickety, although the two children that I have seen die from enlarged thymus were in perfect health. No postmortem was obtained in either case.

In all cases of status lymphaticus the thymus is above normal in size and often the enlargement is very great. Its texture shows little change to the naked eye, but under the microscope there is a

general hyperplasia of the lymphoid elements, associated at times with proliferation of the endothelial cells lying along the trabeculæ of the organ.

Case History. J. W., aged twenty years, was admitted to the University Hospital, service of Dr. Stengel, on December 4, 1924.

*C. C.* Pain and swelling of joints.

*H. P. I.* Apparently well until four weeks ago, when she noticed the sudden appearance of pain and swelling of the left knee. The skin around the joint became tense and purplish and there was exquisite tenderness on pressure. The joint symptoms gradually improved, and a few days later she began to complain of lumbar pains, at the same time developing an acute tonsillitis which subsided in a few days. November 30 she spent all day cleaning windows, resting well that night, but the next morning she noticed that the joints of the left hand appeared swollen, painful and tender; the swelling traveled up the arm. Three days before admission the patient developed another sore-throat, which was followed by a painful and tender hip. The sore-throat gradually cleared up and the hip condition likewise improved, but she was unable to walk.

There is a slight dyspnea on exertion, but no cough, hemoptysis or pleuritic pain. She gives a history of weakness, fatigue, palpitation and spots before the eyes. Appetite has been poor since the onset of pain in the head. Since the pain in her back she noticed occasionally burning pain with urination. There is a history of frequent headaches, localized chiefly in the frontal and temporal region, beginning three years ago, coming on about twice a week and lasting for a day. She has never had fainting spells or convulsions; had night-sweats for a year.

*Menstrual History.* Not excessive; two pregnancies; one child died, aged fourteen days, from pneumonia; one child living, aged seven months; no miscarriages.

*P. M. H.* Patient states that she was a strong, healthy child and had the usual diseases of childhood. When ten years of age she developed bronchial trouble, characterized by fever, tightness in chest and cough, occurring in paroxysms coming on in the spring and fall of the year and each paroxysm lasting about two weeks; attacks ceased after the age of thirteen. During the winter months there have been frequent attacks of sore-throat which kept her from school. There were many abscessed teeth, which her dentist treated locally.

*Physical Examination.* Patient, a young, well-developed, slightly undernourished white woman, aged twenty years. She lies in bed evidently suffering from pain in her left hand, evidently slightly toxic, skin hot and dry, face flushed. There is no cyanosis, pallor or dyspnea. Blood-pressure 120/70.

*Head.* Contour normal, scalp clear, hair abundant. Eyes: No exophthalmos, strabismus, mystagmus or extraoccular palsies; pupils equal, moderately dilated and round, react well; and promptly to light and in accommodation; media clear, disks well defined, vessels not sclerotic or over-

filled, retina good color, no hemorrhages or exudates. Nasal: No obstruction of air-passages, no discharge. Ears: Hearing good. Mouth: Tongue clear and protrudes in midline without tremor; four carious teeth with pyorrhea and gingivitis of mild degree. Tonsils: Markedly congested, enlarged, cryptic and undoubtedly diseased. Pharynx, moderately congested.

*Neck.* No abnormal pulsations, anterior upper cervicals and posterior cervicals enlarged and shotlike; no thyroid enlargement.

*Chest.* Well-developed, symmetrical; expansion good, costal borders flare well and equal, diaphragm descends well by percussion in rear, percussion note resonant throughout; breath sounds vesicular, no rales or friction. Heart: Not enlarged, apex beat palpable in fourth interspace 9 cm. from midsternum; no thrill or shock; RB., $2\frac{1}{2}$ cm.; LB., $9\frac{1}{2}$ cm.; supracardiac dulness first space 4 cm., second space, 7 cm., sounds rapid, regular, forceful and of good tone; first mitral sounds impure, but no definite murmur. Mamma: Small but very pendulous, with little fat; striated skin, the result of lactation.

*Abdomen.* Muscle tone fair; marked striation of pregnancy, with moderate diastasis of the recti muscles; spleen not palpable; lower pole of both kidneys palpable but not enlarged or tender; liver, fifth rib to costal border; no masses or tenderness in abdomen, no hernia.

*Extremities.* Left hand swollen from the radiocarpal joint down, involving all the fingers, especially the middle fingers, thumb not involved. There is redness and local tenderness. The middle- and ring-finger and the hand and wrist are immobilized by the tenderness and swelling. The right foot shows the deformity known as aquinovarus and the tendo Achillis is rather markedly shortened. The biceps and the triceps are normal and equal. The patellar reflex is brought out only on reinforcement. The Achillis reflex is normal, no Babinski or Kernig. Axillary nodes enlarged, particularly on the left; vessels not sclerotic; no cyanosis or clubbing of nails, no edema of the ankles.

December 8. Urine negative but for many white blood cells, many per HPF.

December 10. Blood-Wassermann negative.

December 15. White blood cells, 9000.

December 17. Roots of three carious stumps removed by Dr. Berkheimer.

December 20. Blood-culture taken, negative.

December 26. Sent for tonsillectomy. Anterior pillars touched with 10 per cent cocaine, 4 cc. of 0.5 per cent novocaine, plus two drops of adrenalin, chloride (1 to 1000) were injected into each tonsil. The left tonsil was rapidly removed because the patient became greatly excited. She then began to stiffen, and short, clonic convulsions began. This was from one to one-and a half minutes from the injection of the novocaine. She then lost consciousness and became cyanotic, her respirations were irregular and shallow and her pulse feeble. She became quiet in about a half minute, but when touched her muscles would go into a spasm. She was given strychnine sulphate, gr. $\frac{1}{30}$, but her respirations soon stopped, her pulse continuing for a short time. The whole attack from the time of the injection to cardiac arrest was about three to four minutes. Intercardiac adrenaline,

4 cc., was given by Dr. Shelly. Artificial respiration was continued without effect for twenty minutes.

December 28. A sample of the solution injected was analyzed by Dr. Richards, of the medical laboratories, and was found to be novocaine, 0.63 per cent strength.

Autopsy. Complete autopsy revealed an enlarged thymus which microscopically showed evidence of definite hyperplasia. The aortic lymphatic glands were enlarged, but there was no general adenopathy. Thorough examination of the operative field showed no injury to the adjacent large vessels. No other findings having bearing on the case were present.

In looking through the reports of 43 deaths submitted to the committee for the study of toxic effects of local anesthetics of the American Medical Association, I find that 20 out of the 43 were secondary to tonsillectomies. A few of the reported cases are as follows:

Case I. Male, aged twenty-six years. Tonsils showed evidence of previous inflammation. Apothesin, 0.5 ounce, 2 per cent, into tonsil. Epinephrin, amount not stated. Clonic convulsions five minutes later. Strychnine, nitroglycerine, digitalis, each, $\frac{1}{100}$ gr., ether, 1 cc., at five minute intervals for three doses, pulmotor. Death, twenty-five minutes after administration of apothesin.

Case II. Female, aged thirty-eight years. Morphine, gr. $\frac{1}{8}$, one-half an hour before operation; cocaine, 4 per cent applied to anterior pillars and base of tongue; butyrin, 4 drams, 0.25 per cent, into tonsils. Nervous at once; gasped for breath; convulsions at once. Atropine and strychnine injected; ether inhalations; artificial respirations; camphorated oil. Death within a few minutes. Autopsy: Enlarged heart only.

Case III. Female, aged twenty-four years, sitting. Cocaine, 0.1 per cent, amount not stated. Operation completed. Convulsions within a few minutes; death within one-half hour. Autopsy: Acute hemorrhagic pancreatitis; extreme congestion of organs; status lymphaticus; no cocaine in liver.

Case IV. Female, aged twenty-four years. Tonillectomy, sitting. Cocaine, 20 per cent solution, used to swab throat; procaine, 6 drams, 1 per cent solution, injected. Convulsions and cyanosis in fifteen seconds. Artificial respiration; dilation of sphincter; after which there were cyanosis, convulsions, semidilated pupils, faint radial pulse, scanty respirations. Cardiac massage; ether injected subcutaneously; epinephrin, 1 to 1000, injected into the heart. Death within a few minutes. Autopsy: Status lymphaticus; no cocaine or procaine in liver.

Case V.—Female, aged twenty-six years, sitting. Tonsillectomy for chronic tonsillitis. Cocaine, amount not stated, 10 per cent to swab throat; procaine, 0.5 per cent solution, amount not stated. Convulsions with respiratory and cardiac failure, beginning before injection completed. Death in about four minutes. Autopsy: Status lymphaticus.

Case VI.—Aortic insufficiency, myocarditis, chronic rheumatism. Tonsillectomy, sitting. Cocaine, 10 per cent to pillars; procaine, 100 minims, 25 per cent solution, injected; epinephrin, 5 minims to ounce of procaine. Cyanosis during operation, followed by eight or ten convulsions. Ether; small doses of morphine; camphor; caffeine hypodermically. Death in half hour. Autopsy: Chronic interstitial myocarditis; marked coronary sclerosis; congestion of all organs.

During the last sixteen years I have seen three deaths during or immediately following tonsillectomy, two children and one adult, in the hands of three different operators, and all three patients would probably be alive today had we left them alone or had a proper *x*-ray examination of chest been made. It is now the routine treatment to radiograph all children between one and fourteen years, booked for tonsil and adenoid operation, at the throat department at the Massachusetts General Hospital and Massachusetts Eye and Ear Infirmary.

All children showing a broad superior mediastinum are considered as suspicious thymic cases and are given four *x*-ray treatments of a third of an erythema dose. The treatments are repeated at intervals of ten days. The total number of children radiographed were 2344; of these 185, or 7.5 per cent, showed a positive thymus shadow. Of the 185 positive cases, 110 have been treated and successfully operated upon. Ninety per cent of the children treated showed a diminution of the broadness of the superior mediastinum.

It seems to me that all hospitals who book their cases four to six weeks in advance should have them go through the pediatric department, where a thorough physical examination should be made, including *x*-ray of chest and suggestions as to whether the patient is a fit subject for anesthetic and operation.

FEBRUARY 18

## Lamb's-lung Manikin for Bronchoscopic Study and Practice

BY M. JOSEPH MANDELBAUM, M.D.
NEW YORK

(By Invitation)

The beginner in the study of bronchoscopic technic finds not the least of his problems the obtaining of suitable material for study of the bronchoscopic field. Teachers of bronchoscopy in general, and Dr. Chevalier Jackson[1] particularly, emphasize the dangers attending the use of the special bronchoscopic armamentaria upon the human subject without prolonged, painstaking studies upon both the cadaver and the living dog. Indeed, Dr. Jackson advocates daily practice of one to two hours until several hundred hours have been passed in the use of bronchoscopic intruments for training both the eyes and the hands in the many delicate adjustments and manipulations necessary for the development of a satisfactory technic. Cadaveric material and living dogs not being easily available, Dr. Jackson[2] has recommended the use of a specially prepared rubber tube to simulate the trachea, which is held fast in a small iron vise, providing a simple, always-at-hand manikin for practice at odd moments. While this device permits to a degree a ready means to develop a certain amount of digital dexterity and acquaints one with proper holding of the bronchoscopic tube and intratubal use of the various endoscopic forceps and instruments in their relation to foreign bodies placed within the rubber "trachea," it is not designed to train the eye as to the color and consistency of real animal tissues, or give the student a proper idea of the formation of the trachea at its bifurcation at the carina and the location and direction of the main bronchi and their chief lobar subdivisions. In searching for a better and more natural substitute for bronchoscopic practice, I considered the various materials easily obtainable in all sections, whether large cities or remote towns, and turned to the ruminant group and other "meat" animals most commonly handled by the average butchershop. A comparative study of the lungs of the cow, pig, sheep, etc., led

to the selection of the lamb's lung as most nearly approaching the human lung in its gross anatomy, coloring and dimensions. The ease with which a lamb's lung can be obtained, as well as its neglible cost, led to its final selection for the purpose intended.

Comparative Anatomy of Lamb's Lung and the Human Lung. In size the fresh eight-month's old lamb's lung approaches that of the human lung at puberty. The tracheal and bronchial dimensions are practically the same, as is its mucosal coloring, with the exception of the length of the trachea and thus a difference in the number of tracheal rings. As the distance from the cricoid cartilage to the carina in the lamb is about two and one-half times longer than in the human, there is a corresonding increase in the number of its rings. The rings in the lamb are also somewhat stiffer than in the human trachea, their cartilages being one and one-half times heavier; they also extend almost completely around the circumference of the tracheal tube, there being a very slight dehiscence in the midline posteriorly. The rings also are placed more closely together than in the human, the intervening annular, membranous sections being narrower and slightly thicker. The carina is well developed and the angles at which the right and left main bronchi are given off are quite the same as in the human subject. The number and direction of the main lobar subbronchi vary somewhat from the human.

While the trachea divides at the carina in a dichotomous fashion into a left and a right main bronchus, the extra, superior lobe of the right lung communicates with the trachea by means of an independent bronchus given off about 3 inches above the carina at the right anterolateral portion of the tracheal lumen. This bronchus offers excellent practice for use of the flexible, 180°, curve-ended forceps and the flexible, curve-ended irrigating or suction tube of Lynah, simulating the right upper-lobe posterior branch bronchus. The lobular branches of the subbronchi are more numerous than in the human being.

The texture of the parenchyma is also about the same as in the human lung, as is its histologic structure. The chief morphologic difference lies in the lobar divisions of the right lung, which in the human consists of tree lobes (an upper, middle and lower), while in the lamb's lungs the right is subdivided into four lobes, the upper of which is an adventitious lobe somewhat separated from the one next below, this latter second lobe corresponding in morphology

and topography to the upper lobe of the human right lung. The upper extra lobe of the right lamb's lung lies somewhat superior and internal to the second lobe and is the uppermost of the four lobes and passes anteriorly to the midline, crossing it and curving in front of the heart. The tubal texture and resiliency are also the same as that of the human lung.

An important and advantageous difference lies in the more highly developed elastic structure of the lamb-lung's subserous pleural membrane, as it allows an easier inflation and deflation of the lungs, and retains this elastic property much longer after removal from the carcass than does the human lung. Thus with all these admirable qualities for the purposes of a substitute manikin for human lungs as well as the ease with which it can be obtained, lamb's lung is the ideal practice material for bronchoscopy.

Dr. Jackson[3] well states that "no endoscopist has enough practice on the living subject, because the cases are too infrequent, and furthermore, the tube is inserted for too short a space of time." and that "before attempting the removal of a particular foreign body from a living patient, the anticipated problem should be simulated with a duplicate of the foreign body in a rubber tube. In this way the endoscopist may precede each case with a practical experience equivalent to any number of cases of precisely the same kind of foreign body."

The lamb's lung offers the additional advantage of allowing the placing of a duplicate of the inhaled foreign body in exactly the same location for practice, whether in the trachea, main bronchi or their branches, and familiarizes one with the three essentials of endoscopy, viz., approach, manipulation and grasp. There is no real foreign-body emergency that cannot be duplicated or afford exact practice with the lamb's lungs. As Dr. Jackson[4] states: "It is not only inhuman but impossible to obtain this experience on children." Next to this properly forbidden experimentation on children, the living dog offers the best substitute; but the difficulty as well as expense in securing and caring for living dogs for such experimental endoscopy well-nigh makes impossible for physicians outside of medical university centers the use of this means.

Indeed, with exacting and rigid antivivisection laws and activities of societies for the prevention of cruelty to animals, etc., one hesitates to incur the enmity of and possible prosecution by these agencies. In most communities special licenses for use of living dogs for these purposes are limited to established teaching institutions.

With all these difficulties to contend with, the use of lamb's lung thus commends itself to both the student and specialist for bronchoscopic study. After considerable practice on the lamb's lung I found that the only factor lacking for making it a perfect substitute for living human or dog subjects was the interesting phenomenon observable in working upon living subjects, viz., the dilatation and lengthening of the bronchi during inspiration and their contraction and shortening during expiration. It occurred to me that, with the well-developed elastic membrane of the lamb's lung, it might be possible to construct an apparatus that would allow a mechanical simulation of respiration by inflating the lung to represent inspiration and deflating it to represent expiration. I adapted the foot-bellows, which was connected by means of a rubber tube attached to a small side branch at the upper end of a metal tube so made as to tightly grasp with an air-tight connection the upper end of the trachea with the larynx removed. By this means the fresh lamb's lung can be inflated and deflated at will. While working the floor bellows with one foot, both hands are left free to use the bronchoscope and the various endoscopic instruments as desired or needed for a special problem. The upper end of the metal tube is a separable milled nut holding a soft-rubber diaphragm pierced at the center, and through which is passed a specially constructed practice bronchoscope made so it is tightly grasped by the rubber diaphragm, preventing the escape of air from the trachea.

In addition to simulating specific foreign-body problems by implanting endoscopically, in the various divisions of the lamb's lung, coins, pins, tacks, staples, peanuts, etc., this perfect manikin can be used for the practice of suction and irrigation of lung abscess or bronchiectasis, as described by Drs. Lukens and Moore;[5] endobronchial application of injection of various medicaments (oils, sprays or powder), and also for lung-mapping (insufflation of powdered bismuth subcarbonate into various branches of the bronchi), as developed by Dr. Clerf;[6] for practising with Dr. Tucker's[7] side-grasping pin and tack forceps; for using all the Jackson instruments, and any other known and feasible endobronchial procedure.

Beyond question the most difficult bronchoscopic procedure is the removal of inhaled foreign bodies by the means of biplanal fluoroscopy, as practised by Drs. Jackson and Manges. The indications and opportunities for performing this most difficult of procedures are very limited and the means at hand still more difficult

to obtain. The lamb's-lung manikin offers an ideal subject for the practice of this procedure, the roentgenologist and bronchoscopist being thus enabled to work together at such times as they may elect.

When securing fresh lamb's lung, the party supplying the material should be cautioned that the lungs should be removed with the trachea, bronchi and lungs free from careless cutting of the bronchial tree or pleural surfaces, as such cuts prevent satisfactory inflation by permitting the escape of air. I personally have the larynx, trachea, lungs, heart and its great vessels as well as the esophagus and stomach removed "en masse." This permits of a perfect study of the relative positions of these various organs and acquaints the future endoscopist with their surgical and topographic anatomy as well as the dangers of unskilful endobronchial manipulations. After using, the lamb's lung may be placed in the household ice-box, without fear of contaminating food; carefully handled, a single lamb's lung manikin even in hot weather will serve for a week's study. Before attaching the tube to the upper end of the trachea, it should be evenly cut across, about midway between the larynx and the carina, to correspond to the length of the human trachea.

I wish to thank Dr. Jackson for his kind encouragement in the development of this manikin for bronchoscopic study, and George P. Pilling & Sons Co. for their coöperation in the development of the mechanism needed to perfect the inflating apparatus and the specially constructed practice bronchoscope.

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4. Ibid., p. 122.
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6. Clerf, Louis H.: Bronchoscopic Lung Mapping in Diseases of the Lung, Surgical Clinics of North America, 1924.
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# Closure of Laryngostomic Fistulæ

BY CHARLES F. NASSAU, M.D.

(By Invitation.)

The closure of fistulæ of the larynx and trachea is a problem which presents itself after the laryngologist has completed his treatment of a patient. It is of academic interest only whether the obstruction which preceded the laryngostomy was caused by scar contraction, bilateral recurrent nerve paralysis, gunshot injury or stab wound; closure of the fistula, independent of the cause, is carried out in the same way.

Consideration must be given to the method of anesthesia, which is of vital importance in these cases. A general anesthetic is difficult to administer; furthermore, the respiratory excursions of the larynx during general anesthesia would be embarrassing while introducing the necessarily large number of fine sutures. Coughing, vomiting and the secretion of mucus in the trachea are other disadvantages. Under local anesthesia there is no limitation of the amount of time that may be consumed in operation, and the patient is breathing normally throughout. The 7 patients in this series were operated upon under local anesthesia and only 1 patient complained of pain. The youngest patient in the series, aged eleven years, gave just as full coöperation as the adults. Field block is the method of choice, and novocain in $\frac{1}{2}$ per cent solution, with the addition of 6 minims of adrenalin chloride to each ounce of solution, is the preferred anesthetic. Infiltration of the flap itself is not necessary and should be avoided on account of possible interference with healing.

Heretofore the closure of these fistulæ (Fig. 1) has been a very uncertain surgical procedure, and in about 50 per cent of cases the closure has not been permanent. At the request of Dr. Chevalier Jackson I devised a method which has given excellent results in the patients operated upon in this manner. A number of points must be given careful consideration if the end-result is to be satisfactory. The theoretically perfect operation demand that no narrowing of the air-passage be produced, that the new lining shall consist of skin, that the closure shall be made up of more than a single layer,

that an adequate blood supply shall be present to guarantee the vitality of the reconstructed part and that absolutely no tension on the sutures shall exist after the procedure has been finished. Encircling the fistulous area and inversion of the tract were not considered,

Fig. 1.—Laryngostomic fistula.

as this would narrow the air-passage and the tissues utilized would have a poor blood supply, because they would consist chiefly of scar. To turn back a flap from one side across the fistula would necessitate sutures on three sides of the flap, and the raw area left

by the turning over of the flap from the side is not so easily covered as one taken from the median line. Moreover, this method might leave a line of raw surface on the newly formed anterior wall of the larynx and trachea. I planned, therefore, to bring the flap from below the opening, with its base attached to the lower edge of the fistula. By doing this, skin and fat which have a fair circulation can be secured, and the narrowness of the flap obviates any difficulty in bringing the superficial wound together in the median line. Operation upon patients who are suffering with the slightest degree of bronchitis or coryza must be postponed.

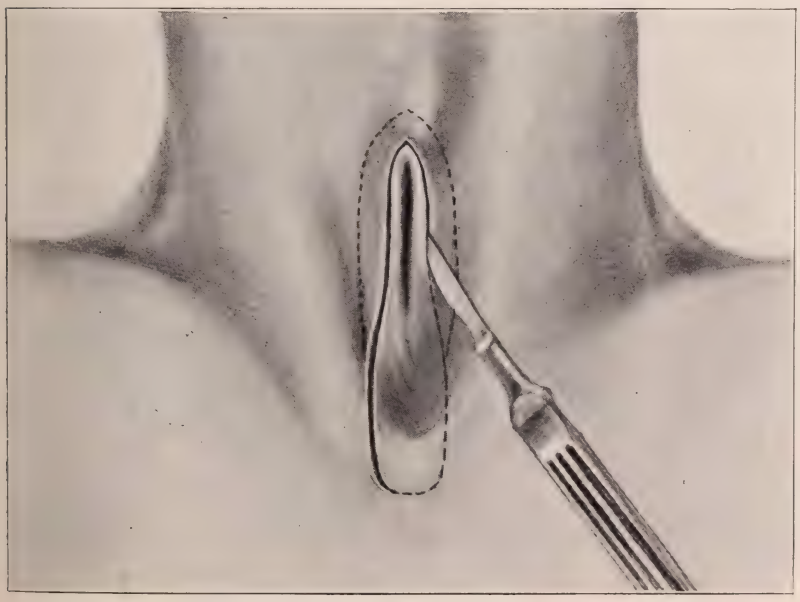

Fig. 2.—Outlining of flap. Dotted lines indicate the area to be undercut.

No special preoperative preparation is necessary. Great care must be used, however, in disinfecting the skin, whether it be with alcohol or iodine, as the dropping of any irritating solution into the trachea produces violent paroxysms of coughing. Any hair existing on the surface of the flap should be destroyed by *x*-ray previous to operation.

The method of operation employed consists in raising a skin flap with its base attached to the lower end of the laryngostomic fissure (Fig. 2). The width of this flap is outlined in such a manner that

the upward prolongation of the incision around the opening is not less than 6 mm. from the edge of the opening. This is a very important point, because if too narrow a flap be cut and the incised edge which is afterward undercut laterally, as shown by the dotted lines in Fig. 2, is made too close to the edge of the opening, the mucous membrane which lines the air-passage will have retracted to such an extent that introduction of the sutures will be a difficult matter.

The length of the flap downward passes beyond the insertion of the tendinous portion of the sternocleidomastoid muscle and at times extends over the manubrium. The width of the flap should be almost the same at the top as at the base, and the flap should not be made pointed. Measure the length of the fissure and add one-third to this measurement to allow for shrinkage. The width of the flap should be 2½ cm. as a rule, although it may be as narrow as 2 cm. Skin and underlying fat are lifted in one piece and the lower end of the flap later corresponds to the upper end of the laryngostomic opening. Ascertain that the flap is sufficiently long to lie perfectly loose over the opening without tension. Undercut the area laterally along the sides of the opening and above it so that the remaining skin of the neck can be brought together in the median line over the flap. The upturned flap is then sutured to the edge of the lining of the opening in such a way that the sutures are invisible from the outside when they are tied, and the knots come to lie on the inside of the air-passage (Fig. 3).

This method of tying the knots is analogous to the end-to-end suture of the small bowel by the Connell method of using interrupted mattress sutures, or to the repair of a complete tear of the perineum where the sutures are tied on the inside of the bowel.

The first suture is introduced 3 mm. from the point of the folding of the flap at its base against the edge of the lining of the area. This suture and its fellow of the opposite side and the last three deep sutures used in the operation are the most difficult ones to insert and tie. Introduce the needle slightly less than 3 mm. from the edge of the skin flap, at the point where it is folded up over the opening, from within outward and then reintroduce it from without inward; this brings the knot on the inside.

After inserting and tying two or three sutures on one side, the next two or three sutures should be placed on the opposite side of the flap, proceeding from the base to the tip of the flap. This

method will keep the flap straightened out in the position in which it will ultimately lie. In inserting and tying these sutures care must be used to bring the skin edge of the flap into perfect epithelial contact with the edge of the opening. The space between sutures should be less than 3 mm.

As the suture lines approach completion a very little opening is left at the upper end, and sharp scissors should be used to cut off the slightly redundant tip of the flap. This does away with too

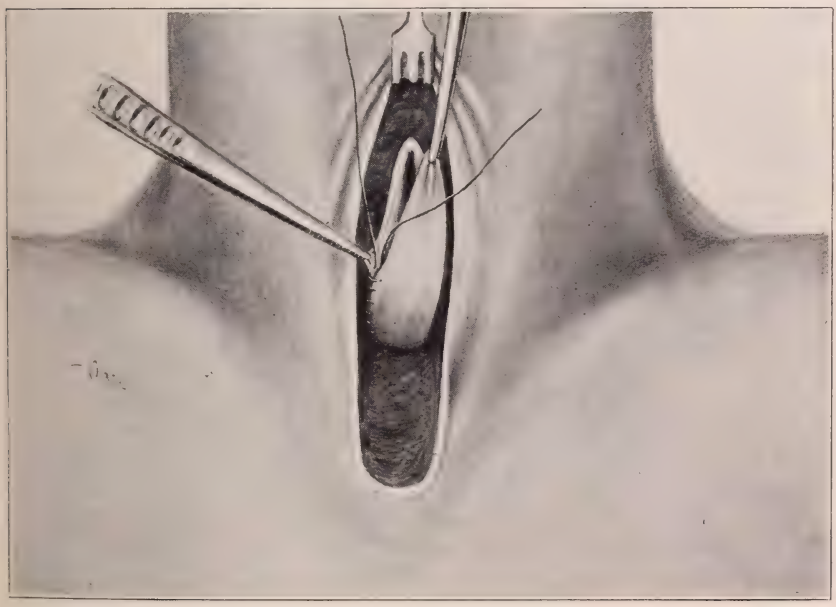

FIG. 3.—Flap turned up and method of suturing.

long a flap and reduces the possibility of gangrene from lack of circulation, and even if it were not necessary for that reason is a wise procedure because it obviates the utilization of tissue that has been held by forceps and possibly devitalized.

The final problem is that of closing a small tube. The last three or four sutures are left untied until all the sutures are introduced. One interrupted suture running from the fat on the top of the flap to the tissues up and beyond the last point of suture will give added security. Interrupted silkworm-gut sutures close

the skin wound (Fig. 4). Be careful not to make too perfect a closure because there may be some infection of the wound and easy exit for secretion should be provided in advance. The space between the sternocleidomastoid tendons is unyielding and the obliteration of a dead space difficult, and a small drain should be introduced at this point.

Ordinary black spool-silk, size A, is used for the deep sutures. Catgut should never be used, because the large number of sutures

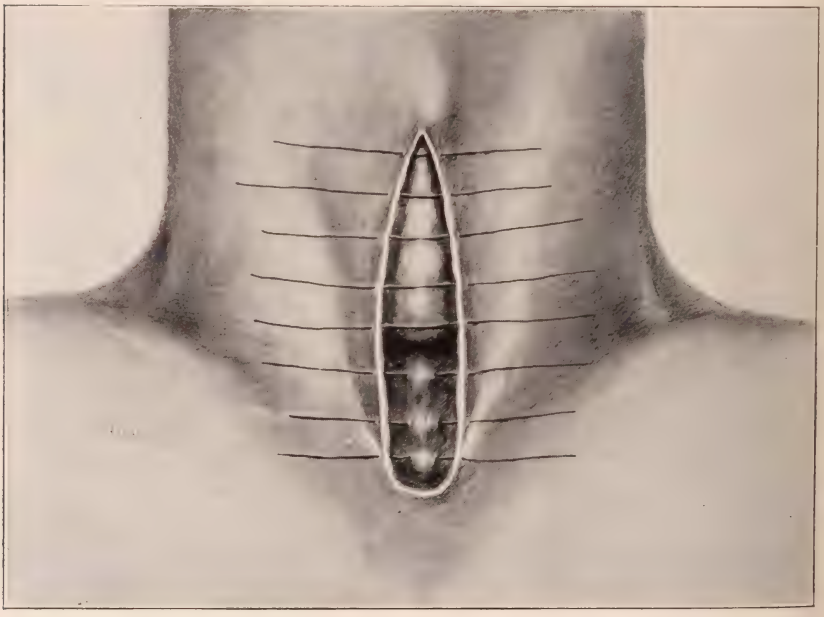

Fig. 4.—Flap completely sutured and superficial wound ready for closure.

of catgut would make a bulky mass of foreign matter which might prove to be decidedly detrimental. The best needle is a milliner's straw needle, No. 9, sharps; it may be necessary to use a very fine curved needle if the skin has been cut too close to the opening, on account of the retraction of tissue.

The principle upon which the success of this operation depends is the security with which the flap is held by the nonabsorbable sutures. The ultimate fate of these sutures need cause no anxiety; they are cast off into the trachea and larynx during the course of healing.

Successful closure depends also upon anticipation of infection. Operation is carried out under extreme difficulties in the observance of thorough antisepsis. Three of our patients developed some wound infection. On the appearance of inflammation hot boric acid compresses are used over a period of twenty-four to forty-eight hours. This treatment saves these wounds from a complete breakdown in the same way that it saves abdominal wounds that are on the verge of infection, as recommended by Watkins, of Chicago. Even if the wound should be very red or should be discharging between the sutures, the skin sutures should never under any circumstances be removed.

The trifling infection in our patients had no bearing on the final result. Six of the patients in the series were referred to me by Dr. Chevalier Jackson. Five of these patients made complete and permanent recoveries. A second tracheotomy was performed by Dr. Louis H. Clerf on the sixth patient on account of scar contraction within the larynx. This contraction occurred six months after the obliteration of the fissure and was not the result of the closure of the laryngostomic fistula. The seventh patient, a lad aged eleven years, who was referred to me from the service of Dr. Fielding O. Lewis, had primary healing and all skin sutures had been removed when on the eighth day after operation, after having been up and around the ward and apparently in perfect health, he died in a few moments of an edema of the lungs, probably attributable to cardiac disease.

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## Case Reports

Dr. Geo. B. Wood presented a case of rhinoscleroma in an adult American male who had never lived outside of the United States. The diagnosis was made by Dr. Allen J. Smith after a microscopic study of biopsy material. Some improvement had been noted in the condition following a series of intravenous antimony injections.

Discussion. Dr. Fielding O. Lewis requested information regarding the exact dosage of antimony used.

Dr. Hunter, who had treated the patient, stated that treatment was started using intravenously 1 cc. of a 1 per cent solution of

tartar emetic, antimony potassium tartrate, and gradually increased until 10 cc. was given. Dr. Small, of the Philadelphia General Hospital, has used this treatment to advantage in cases of granuloma inguinale. The organism present in this condition is a bacillus belonging to the same group as those bacteria found in the lesions of rhinoscleroma.

Dr. N. P. Stauffer referred to several cases of this disease seen by him in Vienna, which on account of extensive tracheal involvement had required tracheotomy.

Dr. Fielding O. Lewis presented the case of an adult male upon whom he had performed a complete laryngectomy on account of laryngeal carcinoma. A month following this operation the patient began to show evidence of infection, pain in the chest and pus in the region of the trachea. A fistulous tract posterior to the trachea was discovered which led to a large abscess cavity, the presence of which was confirmed by *x*-ray. Repeated evacuations of the cavity by means of suction, feeding through a nasal tube and careful nursing were repaid by complete recovery. Dr. Lewis stated that many such abscesses following this operation have been reported and that recovery occurs in about 40 per cent of cases.

Dr. George Fetterolf presented 2 cases illustrating the necessity of careful and thorough study of the patient before attributing the cause of the condition to be tonsillar infection. The first case, a young male, was referred by an internist for tonsil removal on account of a condition which had been diagnosed sciatica. The tonsils showed disease and were removed. A few weeks later a spontaneous fracture of the right femur occurred and an *x*-ray examination showed the presence of a large bone-sarcoma.

The second case was a middle-aged male who complained of neuritis of the right shoulder. Although a certain degree of tonsil infection was present, operation was deferred until an examination of the prostate gland was made. Definite infection was found in this gland and appropriate treatment carried out, after which the neuritis of the shoulder entirely subsided.

Discussion. Dr. A. Randall spoke regarding the ease of prostatic examination and the definite information that can so be obtained. A positive venereal history is not essential for prostatic infection. Even in specific prostatitis after three years the gonococcus is

rarely found while secondary invading organisms may be present in abundance. Nonspecific infection of the gland may arise from: (1) Constipation; (2) trauma; (3) focal infection; (4) sexual excesses. Frequently the infection is not found until the second examination.

Dr. G. Morley Marshall reported the case of an eleven-year-old male upon whom he had performed a mastoid operation for acute mastoiditis. Following this operation a red fungus-like growth appeared in the wound, the identity of which was not determined. Later the wound for several weeks discharged a clear serous fluid which eventually became dry following the use of aluminum acetate.

Dr. E. B. Gleason spoke of tests for the purpose of determining the presence or absence of cerebrospinal fluid.

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MARCH 18

## The Practical Value of the Roentgen-ray in Sinus and Mastoid Conditions

BY FREDERICK M. LAW, M.D.
NEW YORK CITY

(By Invitation)

(*Abstract*)

By personal contact between the roentgenologist and rhinologist or aurist much more can be learned from x-ray studies of the sinuses than if a less intimate relation exists. By verbal consultation the surgeon can make clear the symptomatology in a manner that a written report cannot duplicate. To the interpreter of the *x*-ray films this information is of extreme value, and only after possessing this knowledge can he properly estimate his findings. Technically perfect films are absolutely essential.

A proper reading of such films takes into consideration two main factors: (1) Anatomy; (2) Pathology. Of these two the former is the more important; more important because the pathology

usually is fairly well understood before films are made, but by an accurate description of anatomic conditions the surgeon will be greatly aided in his operative maneuvers. For example, no report of the frontal sinuses is complete unless the observer has stated the size, outline, wall thickness and anteroposterior diameter of the floor of these spaces; no ethmoid report of real value if it fails to give the position of the capsule border, the relation of the posterior cells with respect to the sphenoid or the absence of such cells. In considering the antrum of Highmore the relation of the teeth to this cavity, its size, floor level, wall condition and presence or absence of osseous septa should be mentioned. The same detailed consideration should be given the sphenoid. Mention of the thickness of the cribriform plate is often of value and comfort to the surgeon. In short, all anatomic points that could possibly influence or make more accurate surgical procedures should be stressed.

From the pathologic standpoint the *x*-ray does not reveal much not already known, but it helps to confirm this knowledge and accurately localize the lesion. A film, properly made, will demonstrate the periosteum and the presence or absence of bony septa. Such plates give definite information regarding the acuteness or chronicity of the condition. Chronic purulent sinusitis, for example, shows a demonstrable osteitis of the bony walls; on the other hand, the hyperplastic type gives evidence of an edematous periosteum. Acute conditions cause a lack of definition of the sinus walls, while chronic conditions intensify this particular feature. Quite often an anteroposterior view of the ethmoid cells shows nothing abnormal. A stereolateral exposure of the same patient may, however, show definite evidence of disease manifested by septal absence demonstrable only by such a view. This position, too, gives information of the relation of the posterior ethmoid cells to the sphenoid sinus which is of much value in surgery of that region. In chronic polypoid conditions a peculiar opalescent, milky, gelatinous, glassy appearance is diagnostic.

In the consideration of the mastoid process, its air-spaces and *x*-ray appearance, it is well to know that trivial conditions such as a furuncle of the auditory canal may alter its roentgenographic characteristics. Stereoscopic mastoid films should always be made. Only by such examination can the solution of cell walls in the deeper portion of the cavity be diagnosed if the cortical cells are intact. This is often the case in early mastoiditis. Examination of this

sort has some prognostic value. If large cells are found in the vicinity of the mastoid antrum operation can be longer deferred than if these cells are very small. In the latter case, when mastoid symptoms are definite, it is safest to operate without delay.

In chronic mastoid conditions the information derived from *x*-ray studies is of less value. Cholesteatoma can as a rule, be diagnosed. Whether a sclerotic or pneumatic process is present can be determined. Often in postoperative cases that do not subside following operation, an isolated nondraining cell can be demonstrated.

Discussion. Dr. H. K. Pancoast agreed with Dr. Law regarding the value and necessity of verbal conferences between the clinician and roentgenologist. It is important that the position of the outlying ethmoid cells should be acurately determined.

Dr. W. F. Manges considered it difficult for most roentgenologists to secure the amount of information from sinus films that Dr. Law is capable of obtaining. In many neurological cases an *x*-ray exposure of the entire head is required. Frequently these plates reveal unsuspected sinus or mastoid abnormality.

Dr. G. E. Pfahler considered the experience of Dr. Law in sinus and mastoid work to be greater than that of any other roentgenologist, and consequently regarded him as an authority. He, too, advanced a plea for perfect films. Great care must be exercised in such photography in order to secure cell-wall definition. Without this perfection a proper reading is impossible. He raised the question of radium and *x*-ray therapy of polypoid conditions and asked Dr. Law his experience in such treatment. Dr. Law replied that radium has been used in this condition at the Manhattan Hospital, but the results have not been satisfactory. In his opinion early surgery gives a better chance for cure.

Dr. MacCuen Smith emphasized the necessity of a careful technical interpretation of *x*-ray findings of the sinus and mastoid regions. It was his feeling that many rhinologists and aurists have little confidence in *x*-ray findings because their films have not been interpreted with sufficient detailed accuracy. The position of the sigmoid sinus and emissary vein of the mastoid should always be stated.

Dr. C. E. Eves asked Dr. Law if a diagnosis of hemorrhagic mastoiditis can be made when cell-wall solution does not occur. In this condition sinus thrombosis often follows with little or no cellular destruction.

Dr. Law considers this type of mastoiditis to be the most difficult and unsatisfactory type for diagnosis. It occurs most often in large, fairly well-developed mastoids. There is present a peculiar transparency resembling polypoid conditions, the cell septa are more thin than normal but not lost, and, in the stereoscopic view, deep in the region of the sinus plate they may be absent. If mastoid symptoms are definite and the *x*-ray shows slight osseous destruction, be suspicious of this type of mastoiditis. It is well to *x*-ray on successive days, as bone destruction frequently takes place quite rapidly.

Dr. George Wood raised the question of the nature of the sinus shadow in health and disease.

Dr. Law said that as disease of the mastoid process progresses the sinus shadow becomes more definite, because it is more opaque than the other structures. If, however, softening of the sinus plate has occurred, its outline becomes less distinct. By stereoscopic views it is usually possible to estimate the depth of this sinus.

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APRIL 15

## Studies in the Riverbank Laboratory on the Acuity of Hearing for Air and Bone Transmitted Sound

BY A. G. POHLMAN, M.D.
ST. LOUIS

(By Invitation.)

(*Abstract*)

In the audiometric method of functional hearing-tests we have an accurate gauge of the amount of sound used. Although much knowledge can be gained by the use of this instrument, there are many things not yet fully understood, for—

1. Fields plotted by a curve representing the minimum intensity required to hear various pitches is not necessarily an index of the subjects' auditory power.

2. The relation between air- and bone-conduction curves is not constant for different individuals.

3. The variability of bone-transmitted sound is much greater than that of air.

4. Lateralization tests may vary greatly with the individual intensity and pitch.

In his work upon lateralization tests Dr. Pohlman has found that some individuals lateralize to the affected side. If, however, the intensity is increased, lateralization ceases. Others show results exactly the reverse, in failure to lateralize for the minimal stimulus, with lateralization following an increase of intensity. The audiometer at present is, in the opinion of Dr. Pohlman, a research instrument and not applicable for routine otologic testing.

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## Ephedrine, a New Drug; Its Action Upon the Nasal Mucosa

BY GEORGE FETTEROLF, M.D. AND M. B. SPONSLER, M.D. (By Invitation.)

Ephedrine is new only in the sense that it is for the first time being used in this country. Some 5100 years ago the Chinese emperor, Shen Mung, classified the crude drug Ma Huang, from which Nagai, in 1887, isolated the active principle, an alkaloid ephedrine.

The department of pharmacology of the University of Pennsylvania, in conducting experiments to determine the physiological action of this alkaloid, has found that in dogs, cats and rabbits it uniformly affects circulation, smooth muscle and secretions in a manner qualitatively similar to adrenalin. Dr. T. Grier Miller and Dr. Carl Schmidt were instrumental in securing for Dr. Fetterolf and Dr. Sponsler enough of the drug for testing its action in solution upon the human nasal mucosa.

A group of 17 patients from the wards of the University Hospital was studied. All possessed a certain amount of turgescence of the nasal mucosa. None had nasal discharge, atrophy or other abnormality.

The color and contour of the nasal mucosa, especially of the inferior turbinates, was first noted and recorded. At the same time

the distance from the surface of the turbinate to the septum was measured. Later a 5 per cent solution of ephedrine sulphate was applied to the anterior end of the lower turbinate of one side. The patients were examined frequently during the first ten minutes, then hourly for six successive hours and finally at the end of twenty-four hours.

In each case the mucosa of the turbinate began to shrink soon after application, the maximum shrinkage occurring in an average time of two and one-third minutes. This contraction was not confined to the site of application, but gave general shrinkage of the mucosa throughout the turbinate's entire length. So extreme was this contraction that the outline of the turbinate bone itself was plainly seen. A marked increase of the interval between the septum and turbinate was observed in all cases. The color of the mucosa invariably became paler, but never showed the extreme pallor which usually follows the application of adrenalin solutions. The first noticeable relaxation of the mucosa took place in two hours and thirty-five minutes. Complete relaxation was observed in three hours and seventeen minutes. No cases showed signs of irritation following the application of this solution. The investigators feel that the drug is one of great promise for intranasal use, as it apparently possesses all the virtues of adrenalin and lacks its undesirable sequelæ.

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## A Unique Case of Frontal Sinusitis

BY GEORGE B. WOOD, M.D.

Dr. Wood presented the case of an adult male who developed edema of the left upper lid, localized pain and mild contitutional symptoms following a cold in the head. These symptoms disappeared after a short period of rest in bed, only to recur in a more aggravated manner a short time after getting out of bed. Again rest caused the condition to subside, but recurrence followed his return to normal activities. This time subdermal crepitus was palpable in the left frontal region. The *x*-ray showed the left frontal sinus to be more clear than the right, but the edges on the left side lacked definition. Serological tests were negative.

At operation it was found that bone necrosis of both the anterior and posterior walls of the frontal sinus on the left had occurred. There was extensive dural exposure. The septum between the right and left sinuses was broken down, allowing the right side to become filled with pus and granulation tissue. At the time of the first operation, external drainage only was performed; later an opening into the nose with closure of the external wound was performed. The external wound closed by primary intention, with the exception of a small persistant sinus in the lower portion. The nasal septum, which is markedly deviated to the left, will be corrected at a subsequent operation.

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## The Surgical Treatment of Cervical Adenitis

BY DRURY HINTON, M.D., F.A.C.S.

No disease that comes under the care of the general practitioner can be said to be more important than that of cervical adenitis. The diagnosis of cervical enlargement is easy, but the causes of this increase in size of the glands are so many, diagnostic errors so frequent, and treatment so diverse that a discussion of the problem is in order. In this brief paper we will attempt to clarify the field in a way that will be most helpful to the general practitioner rather than to the surgeon. In gathering material it was necessary to go over records of the past twenty-five years at the University Hospital. The notes on posterior cervical gland enlargement were taken from a survey of the children admitted to the clubs of the Reed Street Neighborhood House, situated in a congested district of this city. Dr. Bothe, of the surgical pathological laboratory of the University Hospital, was kind enough to give certain pathological data referable to the work done in his laboratory in the past two years.

Anatomically the mediastinum is extremely well protected from a descending infection, originating in the head, by a double circle of protecting lymph nodes at the base of the skull, one superficial and the other deep, the deep nodes being really divided into two circles, an upper one and a lower one, joined by two longitudinal

chains, the anterior and posterior cervical nodes, that run along the great vessels and behind the sternomastoid muscle, respectively. Communication between the deep and superficial nodes is free and, in addition, the deep nodes often are in close communication with those of the axilla and mediastinum. On the left side the lower deep cervical nodes are closely in contact with the thoracic duct, injury of which is often fatal. The superficial collar of nodes can be subdivided from the midline backward into: (*a*) *The submental nodes* drain the lower lip, chin, anterior portion of the floor of the mouth and, some say, the tip of the tongue. They lie in the midline and have no relation to any important structures, (*b*) *The submaxillary nodes*, drain the lips, nose, floor of the mouth, gums, anterior portion of the tongue and side of the face. Infections of the lower teeth involve only those glands which lie along the ramus of the jaw. The submaxillary salivary gland, on account of its relatively superficial position, may be removed in mistake for a lymph node, although frequently a node may be embedded in the gland itself. The lymphatics anastomose across the midline. (*c*) *The superficial upper cervical glands*, lying at the angle of the jaw, drain the region of the masseter muscle as far back as the ear. They are involved in lesions of the scalp and skin in the neighborhood The parotid node is constantly associated with tonsil infections. (*d*) *The posterior auricular nodes* lie over the mastoid and are infected from lesions of the ear and neighboring structures. (*e*) *The occipital nodes* are below the superior curved line of the occipital bone, lying between the posterior border of the sternomastoid and the anterior border of the trapezius, frequently extending under the borders of these muscles. A large portion of the scalp is in this drainage area. (*f*) *A retropharyngeal group* lies in the space between the buccopharyngeal fascia and the prevertebral fascia. It communicates with the upper group of deep cervical nodes. Pharyngeal and laryngeal infections and caries of the cervical vertebræ are the usual causes of their enlargement. They do not project forward when enlarged, but promptly form an abscess.

The most frequent causes of enlargement are: (1) Trauma followed by infection; (2) skin diseases, including parasitic ones; (3) colds; (4) disease of the tonsils; (5) dental caries; (6) otitis; (7) syphilis; and (8) tuberculosis. Rarer causes are Hodgkin's disease, leukemia, primary and secondary neoplasm and German measles.

Among the acute enlargements, colds tend to involve the anterior

groups, with prompt subsidence as the cold improves. As a rule, this type of case does not suppurate. This is also true of the type that follows tonsillitis. Suppuration is frequent in the case that follows trauma and infection, and to a less extent in glandular involvement following otitis media. Infection of the posterior pharyngeal group is quite serious on account of the dysphagia, dyspnea and dysphonia that occur, in addition to the danger of death from edema of the glottis, pneumonia or asphyxia from aspiration of the ruptured or incised abscess and mediastinitis from extension of the inflammation. In German measles the disease oftentimes begins with involvement of the posterior cervical glands, a point to bear in mind in differential diagnosis, suggesting the scalp as the source of infection.

The symptoms of acute cervical adenitis are those of any other acute infection. Following acute infection, the glands that drain this area become swollen, palpable, tender, warm, painful and are at times associated with redness, if superficial, or tending toward suppuration. There is commonly edema in the presence of suppuration, and indeed it indicates suppuration in those cases of brawny swelling with the absence of fluctuation, because the glands are lying under the dense deep fascia. Constitutional symptoms are mild or severe, depending on the amount of absorption of toxins. In infections of the superficial glands they may be absent, even in the presence of suppuration; while in deep infections they may be intense, especially where the lower chain of deep cervical nodes is involved or where pus is held in by the deep fascia. In children, high fever is not exceptional even in mild cases, nor subnormal temperature in asthenic old men.

Treatment of these acute infections is aimed at removal or disinfection of the focus, being guided by the exigencies of the given case. Pus, especially if it is under tension or associated with severe constitutional symptoms, should be evacuated. This is done best by the Hilton method, which minimizes the danger of injuring important structures. Retropharyngeal abscesses are good cases for the bronchoscopic clinic. No curetting should be done and no gland removed in the presence of acute inflammation. In the early stage of inflammation local heat by hot compresses, flaxseed poultices or hot-water bottles should be used until the inflammation subsides, localizes or suppurates. In the absence of suppuration the focus of infection should be removed first. If the focus is in the tonsil, a

tonsillectomy should be performed. Following this operation it often happens that there is an exacerbation of symptoms in the glands, which may go on even to rapid suppuration. This reaction is considered by laryngologists to be a favorable sign, both as regards the focus as being the right one, and the prognosis for relief from gland inflammation in the future being favorable. The adenoids drain into glands back of the ear, and their removal sometimes stirs up these posterior glands. In like manner, extraction of teeth when truly the focus of cervical adenitis causes the same exacerbation of symptoms, with prompt relief following. It is fear of this increase of toxic absorption that makes the dentist loath to extract too many infected teeth at one sitting.

In the consideration of the chronic type of cervical gland enlargement the differential diagnosis and treatment are most important. For diagnostic purposes chronic lymphadenitis cases may be classified into those of: (1) Simple chronic inflammation; (2) tuberculosis; (3) luetic; (4) Hodgkin's disease; (5) leukemia; (6) neoplasms.

Simple chronic lymphadenitis has a focus of infection that can usually be readily found by physical examination or history. It is, as a rule, confined to the regional lymph nodes into which the focus drains, at times spreading further by continuity and contiguity. It is frequently associated with a periadenitis and suppuration is not uncommon. The glands are palpable, enlarged, slightly tender and tend to become somewhat adherent to each other and neighboring structures. When the inflammation subsides, the glands as a rule remain palpable.

Witness, for example, in Table I the number of children with palpable posterior cervical glands (63 per cent), presumably healthy children except for the fact that they have or have had pediculosis capitis. Over 90 per cent of these children have perfect teeth and have had tonsils and adenoids removed, with the result that other cervical enlargements are present in less than 10 per cent.

The tuberculous lymphadenitis begins most often in the submaxillary group of glands and tends to run along in chains horizontally, and especially down the anterior cervical chain toward the clavicle. The glands become enlarged, palpable, painless, at first discrete, but as necrosis develops with periadenitis the conglomerate mass of glands becomes fused. Attachment occurs to the skin, and with secondary infection through the skin sinuses develop from one or more broken-down glands. These are hard to heal

with curettage and leave ugly scars. There may be foci of tuberculosis elsewhere in the body.

Luetic lymphadenitis in the early stage is confined to the regional nodes draining the chancre; but later is especially noted in the submental and occipital groups as hard, discrete, not tender or enlarged nodes, painless and freely movable.

Hodgkin's is first noticed at the root of the neck, but later involves other groups of glands, especially the axillary group. Each gland rapidly increases in size, large masses forming like bunches of grapes, there being no inflammation or suppuration, and pain only from direct nerve pressure.

Leukemia closely resembles Hodgkin's or pseudoleukemia, the blood picture telling the story.

Among the neoplasms, primary lymphosarcoma shows the typical rapid growth and infiltrating character of malignancy. The metastatic tumors are usually carcinomatous from drainage tracts above or from upper extremities, breast, mediastinum and occasionally on the left side from the posterior wall and fundus of the stomach.

The treatment of several of these being largely medical can be dismissed in a few words. Syphilis, proven by the Wassermann test and provocative treatment, is treated specifically. Leukemia and Hodgkin's disease are no longer considered surgical other than to the extent of removal of a gland under local anesthesia for pathological examination. *X*-ray and radium therapy are indicated rather than the knife, except as a diagnostic and symptomatic agent. Neoplasms are, as a rule, past hope as far as surgery is concerned, except early and in the submental group, since bilateral drainage anastomosis means involvement wide of the palpable nodes. Preoperative radiation, operation and postoperative radiation offer the best chance. Operation must be a bloc dissection of one side of the neck at a time.

In simple chronic lymphadenitis the effect should first be tried of removal of possible foci. Small palpable glands causing no symptoms should be let alone. Small nests of glands not increasing in size, nor causing symptoms, are not to be touched. Glands in a state of active inflammation should be treated palliatively with hot applications, belladonna ointment, etc., until suppuration occurs, when they should be incised and drained.

Excision of glands should not be performed in the presence of existing acute periadenitis. In supposedly clean cases in which a necrotic gland is opened during the course of operation, it is best to stop the operation, being content to curette and drain the cavity until the resulting sinus has healed. In cases of threatening rupture it is wise to anticipate this rupture by an incision placed in a skin crease and in a position for good drainage. This lessens the resulting scar and prevents the skin puckering seen in cases of spontaneous rupture. Deep drainage of abscesses should be done by Hilton's method, a skin incision, puncture of the deep fascia with a closed hemostat, which is then opened widely and withdrawn. Cultures of the pus should be taken if possible.

In tuberculous adenitis, as a rule, the glands should be removed prior to sinus formation or degeneration; in other words, as soon as the diagnosis is made. In cases of doubt a biopsy may be done. This makes the operation a local one and obviates that horrible operation of bloc dissection with its incision across the skin folds and turning of flaps. In the present adenectomy a small transverse or oblique incision is made over the mass of glands, through skin and platysma, splitting the deep fascia if necessary, and the glands are removed by blunt dissection with curved blunt-pointed scissors, following the natural cleavage planes and clamping vessels as they are reached, before cutting. On the left side, special care is taken to avoid injury to the thoracic duct at the junction of the jugular and subclavian veins. At the middle of the posterior border of the sternomastoid muscle the spinal accessory nerve is looked for and preserved. In bloc dissections it may be necessary, in rare cases, to cut the muscle; if so, it should be done high above or below the middle, in order to preserve the nerve supply. In the cases in Table II at least ten nerves were cut. The anterior chain of glands is frequently adherent to the internal jugular vein, which may have to be resected during the course of the operation. The vagus nerve may be injured unless care is taken to preserve it in stripping the vessels. In the past three years many infections following the closure of cervical wounds have been avoided by packing the wound wide open at the conclusion of the operation and then closing by secondary suture in about three days if found to be clean. Bloc dissection, except in the case of malignant disease, has been supplanted by the use of a number of more or less parallel transverse incisions.

TABLE I.—FREQUENCY OF POSTERIOR CERVICAL GLAND ENLARGEMENT

| Age. years. | 1922 Number examined | 1922 Palpable glands. | 1923 Number examined | 1923 Palpable glands. | 1924 Number examined | 1924 Palpable glands. | Total examined | Total palpable glands. |
|---|---|---|---|---|---|---|---|---|
| 3 . . . | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| 4 . . . | 0 | 0 | 0 | 0 | 13 | 9 | 13 | 9 |
| 5 . . . | 0 | 0 | 0 | 0 | 32 | 23 | 32 | 23 |
| 6 . . . | 9 | 6 | 7 | 7 | 7 | 7 | 23 | 20 |
| 7 . . . | 15 | 11 | 10 | 9 | 5 | 2 | 30 | 22 |
| 8 . . . | 36 | 25 | 6 | 3 | 16 | 13 | 58 | 41 |
| 9 . . . | 36 | 24 | 11 | 7 | 15 | 14 | 62 | 45 |
| 10 . . . | 43 | 23 | 11 | 7 | 21 | 18 | 75 | 48 |
| 11 . . . | 53 | 29 | 10 | 7 | 17 | 15 | 80 | 51 |
| 12 . . . | 60 | 36 | 19 | 12 | 19 | 17 | 98 | 65 |
| 13 . . . | 57 | 30 | 12 | 5 | 20 | 14 | 89 | 49 |
| 14 . . . | 57 | 27 | 23 | 10 | 20 | 14 | 100 | 51 |
| 15 . . . | 42 | 21 | 10 | 6 | 30 | 23 | 82 | 50 |
| 16 . . . | 24 | 13 | 3 | 0 | 15 | 7 | 42 | 20 |
| 17 . . . | 4 | 2 | 1 | 0 | 13 | 7 | 18 | 9 |
| 18 . . . | 2 | 1 | 4 | 3 | 3 | 2 | 9 | 6 |
| 19 . . . | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 |
| 20 . . . | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| Total . . | 438 | 248 | 127 | 76 | 249 | 187 | 814 | 511 |

TABLE II

| | No. cases. | Clinc. T. B. | Conf. by Path. | Bloc Diss. | Adenec. | *S.S. | T.+A. | I. & D. | Hodgkins. |
|---|---|---|---|---|---|---|---|---|---|
| 1901 . . | 7 | 7 | 1 | 4 | 3 | . . | — | 0 | — |
| 1902 . . | 5 | 5 | 2 | 1 | 2 | . . | — | — | — |
| 1903 . . | 4 | 4 | 1 | 1 | 2 | . . | — | 1 | — |
| 1904 . . | 15 | 11 | 2 | 4 | 8 | . . | 1 | 2 | — |
| 1905 . . | 19 | 12 | 3 | 6 | 5 | . . | — | 8 | — |
| 1906 . . | 30 | 12 | 12 | 4 | 17 | . . | 3 | 5 | — |
| 1907 . . | 25 | 21 | 16 | 9 | 11 | . . | 2 | 3 | — |
| 1908 . . | 1 | 1 | 0 | 0 | 1 | . . | — | — | — |
| 1909 . . | 2 | 0 | 0 | 0 | — | . . | — | 2 | — |
| 1910 . . | 15 | 10 | 10 | 6 | 5 | . . | — | 4 | 2 |
| 1911 . . | 35 | 20 | 18 | 6 | 19 | . . | 1 | 9 | 1 |
| 1912 . . | 43 | 23 | 17 | 4 | 18 | . . | 4 | 12 | 2 |
| 1913 . . | 34 | 22 | 17 | 5 | 18 | . . | 4 | 5 | 2 |
| 1914 . . | 21 | 10 | 8 | 1 | 7 | . . | 5 | 6 | 1 |
| 1915 . . | — | — | — | — | — | . . | — | — | 1 |
| 1916 . . | — | — | — | — | — | . . | — | — | 2 |
| 1917 . . | 11 | 4 | 0 | 0 | 4 | . . | 1 | 5 | 2 |
| 1918 . . | 16 | 6 | 5 | 3 | 5 | . . | 0 | 6 | 1 |
| 1919 . . | 26 | 5 | 8 | 2 | 17 | . . | 0 | 7 | 0 |
| 1920 . . | 22 | 8 | 7 | 3 | 11 | . . | 1 | 6 | 2 |
| 1921 . . | 20 | 7 | 7 | 2 | 5 | . . | 3 | 10 | 2 |
| 1922 . . | 26 | 5 | 4 | 0 | 6 | 4 | 2 | 12 | 2 |
| 1923 . . | 38 | 25 | 15 | 3 | 16 | 3 | 1 | 14 | 4 |
| 1924 . . | 31 | 18 | 18 | 0 | 12 | 4 | 0 | 13 | 0 |
| Total . | 446 | 246 | 171 | 64 | 192 | 11 | 28 | 130 | 24 |

* S.S. = Secondary suture.

Table II will give a very good idea of the survey of cervical adenitis in cases that had enough data for comparison. It can be seen that the percentage of bloc dissections has rapidly decreased. Of the 3 done in 1923, 2 were for carcinoma, only 3 of which type of case are listed in this table. It is interesting to note the number of cases clinically diagnosed as tuberculous that were confirmed by the pathological examination. It is a little misleading, inasmuch as the reports showing no giant cells and little or no necrosis, but with lymphocytic hyperplasia, are all diagnosed tuberculosis. There is probably also an error in the number of cases of Hodgkin's disease in the days before the Reed picture was recognized.

TABLE III

| | Teeth. | Teeth and tonsils. | Tonsils. | Scalp. | Ear. | Colds. | Stomatitis. | Measles. | Total. |
|---|---|---|---|---|---|---|---|---|---|
| 1901 | 1 | .. | .. | 1 | | | | | |
| 1902 | .. | .. | 1 | | | | | | |
| 1903 | — | — | — | — | — | — | — | — | |
| 1904 | 5 | 1 | 1 | . | 1 | 1 | 1 | | |
| 1905 | 4 | .. | 3 | . | .. | .. | | | |
| 1906 | 6 | 1 | 3 | 1 | 1 | | | | |
| 1907 | 2 | .. | 6 | .. | .. | 1 | .. | 1 | |
| 1908 | — | — | — | — | — | — | — | — | |
| 1909 | 1 | | | | | | | | |
| 1910 | 4 | 1 | 1 | . | 1 | 2 | | | |
| 1911 | 3 | 1 | 8 | .. | .. | 1 | | | |
| 1912 | 1 | .. | 8 | 2 | 3 | 2 | | | |
| 1913 | 7 | 4 | 6 | .. | .. | 1 | | | |
| 1914 | 1 | .. | 6 | 1 | | | | | |
| 1915 | — | — | — | — | — | — | — | — | |
| 1916 | — | — | — | — | — | — | — | — | |
| 1917 | .. | .. | 2 | .. | 1 | 1 | | | |
| 1918 | 2 | .. | 4 | .. | .. | .. | .. | 2 | |
| 1919 | 3 | 2 | 4 | 1 | .. | 1 | | | |
| 1920 | 3 | 2 | 8 | 1 | 3 | | | | |
| 1921 | 2 | 1 | 5 | .. | 2 | 3 | | | |
| 1922 | 3 | .. | 6 | 2 | .. | 2 | 1 | | |
| 1923 | 5 | 1 | 10 | 2 | .. | 3 | | | |
| 1924 | 1 | .. | 10 | .. | 3 | | | | |
| | 54 | 14 | 92 | 11 | 15 | 18 | 2 | 3 | 209 |

Table III gives a bird's-eye view of the positive foci of infection that might have accounted for some of the enlargements that were called tuberculous.

Table IV is made from data furnished by the pathological laboratory. Discrepancy in figures with other tables is explained by the fact that some of these glands were biopsy specimens of patients

TABLE IV.—PATHOLOGICAL DIAGNOSES OF CERVICAL GLAND SPECIMENS

| | 1923. | 1924. |
|---|---|---|
| Tuberculosis | 17 | 19 |
| Chronic inflammation | 5 | 13 |
| Metastatic carcinoma | 4 | 7 |
| Hodgkin's disease | 4 | 1 |
| Acute inflammation | 2 | 0 |
| ? Tuberculosis | 1 | 2 |
| Endothelioma | 1 | 0 |
| Lymphosarcoma | 0 | 1 |
| Malignant branchioma | 0 | 1 |
| Total | 34 | 44 |

never admitted to the hospital, but sent to clinic for removal of a gland for diagnosis under local anesthesia.

The importance of tonsillectomy in relation to cervical gland therapy was not generally recognized until Ballinger called attention to it about 1910, and it was about four years later that dentistry began the revolutionizing crusade that has markedly cut down the number of cases of adenitis in hospital in spite of a doubling of bed capacity. Due credit must therefore be given to the dentist and laryngologist.

It is, therefore, evident that the trend of modern surgery is to be conservative in the chronic cases, eradicating foci of infection before operation where possible, operating at an early date when an operation is necessary, anticipating complications and, in short, treating glands as helpful friends that need help in turn, in the direction of lessening the load they carry.

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## APRIL 22

THE Section was invited by the Sections of Otology, Laryngology and Rhinology of the New York Academy of Medicine to a joint session, meeting in New York on the above date.

The papers, as indicated in the program below, were presented by the New York members and were discussed by the Philadelphia guests.

Papers presented: Demonstration of artificial larynx, Dr. John E. Mackenty; Maxillary sinusitis of oral origin, its diagnosis, occur-

rence and a method of rapid cure, by Dr. Henry S. Dunning; Clinical significance and diagnostic value of the tuning fork tests, by Dr. Arthur B. Duel; Clinical significance of the newer tests for hearing, by Dr. Edmund P. Fowler (by invitation); A method of barrage anesthesia for mastoidectomy, by Dr. Isidore Friesner.

About twenty-five members of the Section attended the meeting in New York.

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## MAY 20

THE Section substituted for its regular monthly meeting in May an annual Section dinner.

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## OCTOBER 21

### SUBLINGUAL CELLULITIS FOLLOWING TONSILLECTOMY

BY GEORGE FETTEROLF, M.D.

(*Abstract*)

CASE. Three days following tonsil removal under general anesthesia, the patient, a woman of middle age, began to complain of right-sided throat pain; two days later, moderate swelling of the neck, floor of the mouth and tongue developed, with marked edema of the epiglottis. The leukocyte count was elevated to 10,100 and the temperature rose to 3° above normal. For several days the swelling slowly increased. A tracheotomy was averted by spontaneous resolution of the cellulitis following external heat applications and the use of alkaloid sedatives. It was the feeling of Dr. Fetterolf that the most plausible explanation of the condition was thrombosis of the lingual vein by extension from the tonsillar plexus with concomitant stasis of the lingual, sublingual and superior laryngeal veins.

# Case of Tonsillar Vertigo and Asthma

BY WILLIAM A. HITSCHLER, M.D.

This patient was inherited from a distinguished colleague whose notes often displayed a penmanship confirming the ancient and more or less honorable tradition of the layman; so that some of the data will remain obscure; but at that it will not seriously interfere with a brief study of the case.

Case History. Man, aged sixty-three years, first came under my observation early in 1920, suffering from an otorrhea with cholesteatoma. He had scarlatina when a child and the otorrhea was an infrequent and an apparently harmless heritage. That there were granulations, pain and an odorous discharge may sound sinister enough, and sufficiently so to account for the vertigo, if not for the asthma. Local treatment relieved the aural condition but seemed to have no effect upon the vertigo or asthma. There has been no return of the otorrhea since 1921.

The first attack of vertigo occurred in 1918 and was rather severe. No apparent cause was noted. There were nausea and some loss of equilibrium, but no increase in deafness. After this first attack and up to the period of relief the "vertigo" was of irregular occurrence, days or weeks elapsing between attacks. It was never again severe. It lasted but momentarily, was attended by no loss of consciousness, caused but slight annoyance and seemed to be associated with no other symptom or condition. The attacks occurred while lying in bed, as well as when erect and in motion. Examination by an internist and an oculist disclosed nothing that could be regarded as suspicious from their view points.

The asthma dates further back than the vertigo. It was also of irregular occurrence, but gave much more annoyance. It always began with an irritation in the pharynx, chiefly the left side; it was paroxysmal, worse at night and when he had a cold. The duration of the attacks varied from a few minutes to several hours. They frequently occurred about four o'clock in the morning and lasted until six, and of all the remedies tried whisky gave him the greatest relief. The asthma was perennial and independent of any seasonal influence. Protein tests were negative; likewise examination by his internist.

In the fall of 1922 considerable cheesy detritus was found in the faucial tonsils. From then on every local treatment included cleansing of the tonsil crypts by lavage and compressed air, together with the application of tincture of iodine or nitrate of silver. After a few months of such treatment he observed that his vertigo and asthma were quite improved. The association of these symptoms with the tonsilar treatment suggested a

possible etiological factor. I had had a case of vertigo a few years previously which was completely relieved by a tonsillectomy, and other observers had reported similar cases. The patient's age, however, made me hesitate at a complete operation, especially as the family were not favorably inclined. As a compromise the plan of biting away the cryptal walls under local anesthesia was adopted. There were five or six sittings. At the last sitting, June, 1923, there was considerable hemorrhage and further operative work was discontinued.

A moderate amount of tonsil tissue still remains. Occasionally some of the enlarged remaining crypts contain a small amount of detritus, but they are usually free. Since the operations, however, the vertigo and asthma have become progressively and rapidly better and better, and at the present time they have virtually disappeared.

This patient has had and still has nasal obstruction, due not to any marked deformity or disease, but chiefly to a dolichocephalic skull; is subject to acute attacks of nasal-sinus disease and to gastrointestinal disturbances; he has pyorrhea, and his right upper second bicuspid tooth, abscessed previous to 1922, was not removed until July 1925; he has a history of otorrhea since childhood and the otorrhea ceased four years ago with no other symptomatic change than a noticeable improvement in hearing; he presents no history of tonsil trouble at any time beyond a slight pharyngitis when he has a nasal cold; his vertigo began in 1918 and his asthma an indefinite number of years before that; these two symptoms presented no particular variation until the faucial tonsil crypts were in major part destroyed two and a half years ago, following which the vertigo and asthma have practically disappeared. It seems reasonable to conclude that the disease tonsils were the etiological factor. But even so, we cannot be positive about it.

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## Case of Intranasal Osteoma: Operative Removal

BY AUSTIN T. SMITH, M.D.

(By Invitation.)

R. T., white, male, aged twenty-eight years, was admitted to the Jefferson Hospital to the service of Dr. Fielding O. Lewis, July 7, 1925, complaining of complete obstruction of the right side of his nose. His family history was negative. His past history showed excellent general health and only the more simple infections of childhood. There was no history of lues.

The nasal obstruction was first noticed about three months previous to admission. It was at first partial, but after a week or two became complete. The left side was free. There was no history of discharge or epistaxis, and no pain, headache or discomfort aside from that due to the obstruction.

There were no symptoms referable to the ears or eyes. The general physical examination was negative as to any systemic disease. Urine and blood Wassermann were negative.

Upon examination of the nose the right side was found to be completely occluded by a reddish, granular-looking mass. Examination with a probe revealed a very hard substance, which was firmly fixed and unyielding. It was superficially covered anteriorly by dark reddish tissue which bled freely when touched. When this was removed a smooth grayish surface was found which had the appearance and consistency of stone. Palpation in the nasopharynx showed that the mass extended through the choanæ and was of similar hardness posteriorly. It completely filled the right nasal chamber. The left side of the nose appeared normal. The septum was fairly straight anteroposteriorly, but bulged somewhat into the left nasal cavity, due to pressure from the mass on the right side. *X*-ray examination presented a very interesting and unusual picture.

The following is the report made by Dr. Leon Solis-Cohen: "I believe there is a large bony growth, ovoidal in shape, occupying the entire right nostril and spreading into the posterior nasal space on the right side. The nasal wall of the antrum has been pushed outward and the roof of the palate downward by pressure. Its point of origin is uncertain, but we believe it to be somewhere in the ethmoidal spaces. It is of even density and rather well circumscribed on all its borders. In our experience it is the largest we have seen."

*Operation.* The problem of removal was rather a difficult one. To remove the mass as a whole would require quite a radical operation and probably leave the patient with unsightly scars or a nasal deformity. Therefore, it was decided to at first attempt to break it up through the anterior nares so as to reduce it in size sufficient for extraction. This proved much more difficult than was anticipated. The mass was so large and pressed so tightly against the walls of the nasal fossa that it was impossible to get around it with any kind of a crushing forceps. An effort was made to break it up by using a dental engine and drill. However, it proved to be so dense and hard that the best that could be done was to remove a very small specimen sufficient for pathological examination.

Conservative measures having failed, a more radical procedure was necessary. There were two methods of choice: One, to split the nose externally and do a lateral rhinotomy; the other, to enter the nose by way of an incision under the upper lip. Dr. Lewis decided upon the latter, as it seemed likely to give no scarring and a better cosmetic result.

The operation was done by Dr. Lewis under ether anesthesia. An incision was made beneath the upper lip and the nose retracted upward. The cartilaginous setpum was divided near the floor of the nose and pushed to the left. The lateral nasal wall had been obliterated by pressure from the mass and it was necessary to open into the right antrum in order to get around it. By means of chiseling and forcible manipulation with powerful osteroclasts the mass was finally loosened so that it could be rotated and the smallest diameter brought to present anteriorly. A portion of the superior alveolar margin of the maxilla was then removed in order to enlarge the

pyriform aperture to allow passage of the mass. By the exertion of great force and axis-traction the mass was finally delivered. Bleeding was profuse, but was readily controlled by an iodoform pack, which was left in place for twenty-four hours.

The tumor was found to be of the nature of a bony growth. Its surface was light gray in color and relatively smooth. It was somewhat nodular and measured 6 by 4.5 by 3 cm. and weighed 65 gm. Its point of attachment could not be definitely determined. The entire growth seemed limited by a very thin, fibrous capsule. However, it is believed there was a small pedicle attaching it to some point in the lateral wall of the nasal cavity, and this was broken away by the vigorous rocking and prying necessary in the removal of the growth. Due to the encapsulated appearance, it is probable that the growth was entirely removed. There was no evidence of any additional tumors.

In spite of the forcible manipulation necessary, very little injury was done to the normal nasal structure. The cartilaginous septum was destroyed and the perpendicular plate of the ethmoid and the vomer were dislocated to the left side. A large opening was made through the right naso-antral wall.

The patient made a rapid and uneventful recovery, with primary healing of the wound beneath the upper lip. For about two weeks following the operation there was marked crusting of the large cavity, with considerable offensive discharge from sloughing tabs of tissue. This rapidly cleared up under simple saline irrigations and oil sprays.

Due to the loss of the support of the anterior part of the septum and the cartilaginous bridge, the patient now has a nasal deformity of the saddle-back variety, with broadening of the alæ and flattening of the tip. The bony framework is entirely intact and the posterior part of the septum has moved back to the median line. It is planned to correct the deformity at a later date by means of a plastic and rib transplantation.

The tissue diagnosis of the specimen submitted to the laboratory was as follows: "The specimen consists of a large, roughened piece of tissue, bonelike in appearance, measuring 6 by 4.5 by 3 cm. The mass is nodular and brown in color. It saws with great difficulty and the cut surface is gray. Three sections were made for histological examination: Two of them, when examined microscopically, are found to consist of compact bone; the third resembles cancellous bone. The bony ridges are separated by a loose fibrous-tissue stroma containing a few bloodvessels and mononuclear cells. A similar tissue covered one surface of the third section." Diagnosis: bone.

Many bony tumors have been described as arising from the ethmoid, frontal and superior maxillary bones, projecting into the cranium, frontal sinus, orbit, antrum or nares. Those arising from the ethmoid are the more frequent. The next in frequency are those arising from the frontal. In most of the cases reviewed the involvement was of the orbit, frontal sinus or cranial cavity. In none was such a large growth limited to the nasal fossa.

W. L. Culbert collected a series of 215 cases, which represents approximately all the cases of osteoma of the accessory sinuses in medical literature from 1748 to 1918, and his report seems to be the most exhaustive on the subject in the English and American literature; 50 per cent of these tumors were noticed during adolescence and 30 per cent more before the thirtieth year of life. They are generally of slow growth, the development covering a period of ten years, and sometimes much longer, before the annoyance causes the patient to seek relief. Although histologically benign they are clinically malignant, since if left alone they exert ruthless compression into the cavities of the orbit and cranium.

The definite etiology as in all neoplasms has not been determined. Several factors are thought to play a part: external trauma, embryonic genesis, or a combination of both. They may be composed of either the compact or cancellous type of bone. The former is the more usual and in consistence may be like ivory.

The only treatment is complete removal. If not entirely removed, they recur; sometimes in a surprisingly short time. In one case, reported by Thomas, one year after extirpation the tumor had grown to twice the size it was before operation. It is an encapsulated tumor, and the safety and success of the operation for removal depend upon shelling out the tumor from its capsule. With early operation the prognosis is favorable.

The *x*-ray is today our best means of information as to form, location and size of the tumor.

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## Acute and Chronic Mastoiditis with Atypical Lateral Sinus Thrombosis

J. CLARENCE KEELER, M.D.

In presenting the subject of acute and chronic mastoiditis we can hope to offer nothing new simply repetitions; but if by these repetitions the greviousness of a discharging ear shall become deeply and universally impressed, we will most willingly reiterate the importance of giving painstaking consideration both to its subjective and objective symptoms, to a respectful review of the history

of its cause, its onset and duration, the character of the pus; whether the discharge is constant or intermittent, if pain is associated, general or localized headache exists, if dizziness is persistent and the degree of vertigo.

Practically in every case of middle-ear and mastoid infection there is, to a certain degree, evidence of septic infection, because of the venous communication with the lateral sinus. The absence of pain in the ear and over the mastoid is deceptive and unreliable as to the true condition of the underlying structure The discolored, foul-smelling discharge, indicating bone necrosis, may be profuse, scanty or intermittent. Awaiting the much over-estimated classical symptoms, "redness, tenderness and swelling over the mastoid" to appear, serious sinus infection, a thrombophlebitis, may be insidiously forming and it may not give rise to the usually high intermittent fever and chills with profuse sweats; rather, it may be the atypical type of lateral sinus infection presenting few symptoms. Meanwhile the patient has become so profoundly toxic that death may ensue, the true condition not being recognized by the attending physician. A study of the blood picture is of the utmost importance and the roentgenogram is indispensable in diagnosis and in determining the course of treatment. It may be asserted, however, beyond fear of contradiction that surgical intervention is invariably imperative.

In illustration, permit me to review the history of the four atypical cases before us:

Case I.—A. B., male, aged forty-three years. Diagnosis, acute purulent otitis with acute mastoiditis complicated with thrombophlebitis of nine weeks' duration. Returning from a fishing trip, during which he had been directly exposed to the burning rays of sun, he suffered an earache, attributed to the draught in his open car. He had constant, terrific pain, three days and three nights, until somewhat relieved by the spontaneous rupture of the eardrum. The following nine weeks he was under continuous medical treatment, until finally he collapsed. At this stage he was entered at the Jefferson Hospital with the history of having had a chill. Temperature, 102°; leukocytes, 8800. Culture: No growth after three days.

July 3, 1925. *Operation*, a simple mastoid. The cells are to great degree broken down. The bone covering the sinus had become disintegrated. There is a large perisinus abscess. The vessel-wall is covered with protective granulations. There is a clot in the lumen of the vein. It is decided not to disturb the granulations or to remove the thrombus, especially in the absence of more pronounced clinical symptoms, and having had similar cases in which the clot was not removed. Evidently the infection is not of a virulent type and it is considered advisable to await further symptoms.

The postoperative progress is very favorable. The temperature dropped to normal and has remained. There had been no return of the chills. The sinus wall ruptured externally and the disintegrated clot finds exit through the mastoid wound. The watchful waiting policy is not advocated. The patient is prepared to return to the hospital immediately should symptoms arise requiring further observation and intervention. Culture showed no growth after three days' incubation.

NOTE. This case of mastoiditis reached its advanced stage associated with a thrombosed vein while waiting for the classical symptoms to appear.

Specimen of culture from mastoid region, received October 19, 1925: Smear shows a Gram-positive diplococci, a few of which formed short chains. The culture, after twenty-four hours' incubation on blood medium, Staphylococci albus. In boullion and on palin agar, after forty-eight hours' incubation at 37° C. a growth of Gram-positive bacilli resembling diphtheroids developed. (Gamble Laboratories, by M. E. Gamble.)

CASE II.—M. G., female, aged seventeen years, had had a chronic purulent otitis media with chronic mastoiditis as a sequel to typhoid fever in childhood. The ear has discharged a thick, yellow, foul-smelling pus until a year ago. At this examination there is an acute exacerbation of the discharge. A tonsillectomy for the relief of the chronic otorrhea had been performed, but without relief. There is a continuous severe pain on top of the head, increased by pressure over the mastoid. The patient is in a dazed condition. The cerebration is so impaired that the hearing tests are unreliable. Although having received medical attention, both private and in dispensaries, she had not been relieved of her unfortunate suffering. There is no elevation of temperature, nor has she had a chill. There is an organic heart lesion and a rapid, intermittent pulse. The pupils are widely dilated.

December 15, 1924. *Operation*, radical mastoid. The cortex is partly sclerotic and porous in other places from which blood oozes. The antrum is large and filled with granulations. Cholesteatoma and pus under pressure through the entire mastoid. The eardrums and ossicles are obliterated. There is a small necrotic dural exposure in the posterior superior portion of the mastoid. There is a necrotic exposure of the lateral sinus, revealing a perisinus abscess. The vessel wall is collapsed and disintegrated into a grandular formation of connective tissue around which pus seeps.

In the absence of pronounced acute septic symptoms, such as chills and fever, the old sinus wall is not disturbed, although a large area of the cerebellum is exposed for the benefit that might be derived by a cerebellar decompression.

The mild mental confusion and delirium continued several days following the operation. The postoperative recovery is rapid and uneventful. Complete dermatization occurred in about eight weeks.

NOTES. (1) This patient would no doubt have perished before presenting the so-called classical symptoms of mastoiditis. (2) The collapsed, disintegrated, fibrous, sinus wall indicates a thrombosed vessel of long duration. (3) There was an absence of the usual septic symptoms notwithstanding the large area exposed to infection.

Case III.—H. L., male, aged thirty-one years, has had a chronic purulent intermittent discharge from the right ear since boyhood, but at present is quiescent. There is some tenderness over the mastoid. At times, there is sudden vomiting, "cerebral." The rapid elevation of temperature to 103°, with sweats and rigors, suggests pyemic infection. He is listless, very septic and his skin is of a bluish-gray color. He complains of severe headache and pain in the back of his neck. He is not confined to bed. There is very slight discharge. The malleus is present. The posterior half of the eardrum is destroyed. Particles of cholesteatoma are removed through this opening. The hearing is practically lost.

September 9, 1925. *Operation*, radical mastoid. The periosteum is very adherent; cortex eburnated, thick and irregular. Directly under the cortex is a light, glistening mass, which is an accumulation of cholesteatoma eroding through the cortex. The entire cellular structure of the mastoid is destroyed and the cavity is packed with the largest amount of cholesteatoma. The lateral sinus is obliterated, except for the irregular, granular end on the posterior border of the mastoid. The entire base of the petrous is destroyed, the bone being absorbed by the existing pressure necrosis, allowing a free view of the lateral surface of the cerebellum. A right-sided, subtentorial, cerebellar decompression was performed, at which time the dura was found to be white and glistening, owing to the fibrous change. There was also an erosion through the middle fossa the size of the finger nail, over the tegmun antri. The destruction of the osseous structure is so great that the horizontal canal was not located. The cholesteatoma erodes through the posterior meatal wall into the petrous pyramid under the facial nerve, lying exposed in this cholesteatomatus mass. The nerve is thickened and appears somewhat edematous. Touching the nerve, which is exposed for $\frac{5}{16}$ inch, with the edge of the curette, causes the side of the mouth and face to twitch. The promontory does not appear to be involved. This patient is now making uninterrupted recovery and has left the hospital.

Notes. (1) This patient could not have received his shower of infection through the lateral sinus, because it had long been completely obliterated. (2) It is interesting to note the general absence of cerebellar symptoms, notwithstanding the large area exposed to considerable pressure. (3) This patient showed septic absorption of long duration, originally through the diseased mastoid, without presenting the classical symptoms of such infection.

Case IV.—J. G., man, aged thirty-five years, has chronic purulent otitis as sequel to measles in childhood. His chief complaint is pain in the occipital region and back of the neck. Numbness of the right side of the tongue, of the right arm and of the right leg. Defective speech. Vomiting without nausea, and inability to go about without assistance.

There is paralysis of the muscles of the right eye, the right side of the face, the right side of the tongue and the right leg. The speech is impaired. The face asymmetrical. There is some muscular atrophy of the right leg. The knee-jerks are more marked on the right side. Wassermann blood and spinal fluid are negative. The eyes show the disk margins slightly

blurred. The veins are full, but not tortuous. The roentgenogram of the right mastoid shows the mastoid to be the chronic type, with bone defect in the antral region.

The otoneurological examination shows the right labyrinth is dead. There is spontaneous nystagmus in the four directions, *i. e.*, up, down, right and left. There is spontaneous past-pointing of the right arm. Romberg is double plus. He cannot stand or walk without assistance. Stimulation of the horizontal semicircular canal by rotation finds him unable to past-point inward (to the left) or inward with the left (to the right). This indicates involvement of the inward pointing center of the right arm in the right cerebellar hemisphere, and the inward pointing center of the left arm in the left cerebellar hemisphere, which is apparently involved by pressure. The patient's headache became so intense that further examination could not be made.

It is reasonably clear this patient with severe occipital headaches, projectile vomiting, distressing vertigo and spontaneous nystagmus past-pointing and falling, the marked incoördination of arms and legs, the inward pointing centers of the right and left arms, the right-sided paresis, all in conjunction with the chronic otorrhea of the right side, strongly suggest right-sided cerebellar involvement.

May 3, 1919. *Operation*, radical mastoid. Evacuation of a cerebellar abscess with complete obliteration of the lateral sinus of the right side. The entire mastoid is filled with cholesteatoma, pus and granulations. The fascial nerve is exposed by necrotic erosion. The labyrinth is a sequestrum which could not be removed for the laceration of the facial nerve.

*Postoperative Notes.* Slight facial paralysis. The face was assymmetrial prior to the operation. The speech has returned, and he is entirely free from headaches. The inward pointing centers of the right and left arms have resumed their normal function and the spontaneous reactions are no longer present.

Notes. Truly this case is atypical in every sense the term implies. Operation before complications arise is surely the safest course to pursue in warding off such a dire state of health.

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## Operation upon the Sigmoid Sinus

BY CURTIS C. EVES, M.D.

In operating upon the lateral sinus a most important necessity is to provide plenty of room in the bony mastoid cavity. Especially posterior to the sinus should the cells and cortex be lowered so as to give ample opportunity for free use of the instruments from this direction. The posterior cells and the cortex can be best shelved

backward by use of a large, broad-nosed rongeur, being careful in the region of the mastoid emissary not to tear this vein. The final thinning of the bone over the sinus groove is best accomplished by the use of a broad curette; this instrument may be used to remove the initial portion of the sinus plate by thinning the bone over the knee until the vein appears. A more rapid and accurate method of uncapping the knee of the intact sinus is with a flat chisel, beginning from behind. The flat surface of the chisel is placed against the sinus groove at the knee with just enough elevation of the handle to cause the sharp edge to slightly engage the bony plate when chisel is lightly tapped. The bone thus engaged is lifted by lowering the handle and carefully removed with forceps. Sufficient bony plate is removed, by repeating the above, to allow the introduction of the lower blade of a small, blunt, curved rongeur.

Before continuing the removal of the bony plate, it is well to pass a blunt dissector between the bone and vein for a short distance to detect and, if found, to break up any adhesions.

The remainder of the bone can be more quickly removed with safety is a small, curved rongeur with rounded, blunt tips is used. The lower blade is carefully introduced underneath the bony plate for a short distance, thus acting as an additional dissector by pressing the vein away from the bone. Before the bite is taken, the forceps should be slightly retracted to prevent pinching of the vein. The forceps should be made to bite clean through the bone. If the bone is partly cut through and rongeur handle used as a lever to break the remainder, the rough edges may penetrate the sinus wall.

The full area of the sigmoid sinus should thus be exposed, from above the knee to the anterior curve below, before the sinus enters the bulb, and throughout the width of the sinus.

Extreme care should be exercised in the above procedure, as an accidental opening of the sinus or emmissary vein before it is freely exposed may cause considerable difficulty in continuing the operation.

Having exposed the sinus and determined to open the vein, it is always best to make a free incision, as only in this way can the inside of the sinus be inspected and small clots discovered.

Several small, hard-rolled pledgets of iodoform guaze, about the size of a leadpencil and about $\frac{3}{8}$ inches in length should be prepared to control the bleeding. It is advisable to have several larger pledgets of iodoform gauze folded on the flat, about 1 inch square

and $\frac{1}{8}$ inch thick, for emergency. An assistant, with a pair of dressing forceps in each hand, holds the rounded pledgets of gauze in the tips of the forceps at the upper and lower extremities of the uncovered sinus, ready to exert pressure should bleeding occur when the sinus is opened. The sinus is now opened with a scalpel by making a short incision in the center of the outer wall If bleeding does not occur, no pressure is made and the incision extended in both directions with a pair of blunt-pointed scissors. If free bleeding occurs at the time of the first incision, pressure is a once exerted above and below by the assistant, after which the surgeon enlarges his incision as above and dissects away the outer walls of the exposed vein. The pressure from the upper end is then gradually released, and, if bleeding occurs, time enough (two or three seconds) is allowed to determine if the bleeding is free and normal. If so, this end of the sinus is plugged with iodoform gauze. If bleeding does not occur from the upper end, the bony wall covering the sinus toward the torcular should be removed further and the sinus opened until the clot is found. In this way the operator makes an open wound, allowing himself full view of the field and giving much better chances for drainage, than by blindly trying to remove the clot. After the upper end has been treated the plug at the bulbar extremity should be released. If free bleeding does not occur, the clot should be removed carefully with a blunt flexible-shanked curette, or with the ingenious suction apparatus devised by Day[1] for this purpose.

No attempt should be made to remove the clot from the bulbar end without first ligating the internal jugular vein. If bleeding does not occur from the bulb after careful removal of the clot, a narrow strip of iodoform gauze is inserted into the bulb from the mastoid wound, which acts as a drain and should be replaced daily until healing takes place.

When free bleeding takes place it is best not to remove the dressings for six or seven days, unless unfavorable symptoms develop. If the dressing is removed, earlier troublesome bleeding is apt to occur.

If the infection in the bulb is so severe as to warrant, the bulb may be exposed by connecting the incision in the neck with the mastoid wound and the bulb entered. Fortunately this formidable operation is rarely necessary.

Ballance[2] advises bringing the upper end of the divided jugular vein out through the wound in the neck, thus giving a natural drain downward, from the bulb. He also advises against leaving the ligature upon the upper segment of the vein for more than a few hours, as it may become a "test-tube of pus" and may infect the petrosal and so the cavernous sinus.

Through-and-through irrigation is advised by some authors. In cases where infection persists in the bulb, daily attempts are made by placing the tip of a syringe containing normal salt solution into the end of the vein, which has been brought out through the wound in the neck, and, by exerting gentle pressure, endeavoring to cause a flow upward through the bulb into the mastoid wound.

Little more can be hoped for in this method than from drains placed in the bulb from above. The discomfort to the patient and the danger of disseminating the infection have always seemed to me to overshadow any benefit which might be derived from it.

*Treatment of the Jugular Vein.* Theoretically, the jugular vein should be ligated before any manipulation of the infectious sinus. The cases are unfortunately rare in which the experienced surgeon can diagnose infection of the sinus before inspection and incision. Even inspection of the sinus, except where ulcerations of the walls are found, cannot positively determine disease of the interior. In only 2 of 38 cases have I ligated the jugular before opening the sinus, and, while these cases recovered, in the light of my present experience I should not feel the same competence. I have never observed unfavorable results in cases where inspection of the interior of the sinus was first made. Many times, where infectious sinus thrombosis is suspected at the time of operation, the judgment of the surgeon prompts him to wait a few days, which can usually be done without harm to the patient, before ligating the jugular vein.

Identical symptoms, *i. e.*, septic temperature, chills, positive blood culture, etc., can be caused by obscure intercurrent disease complicating mastoiditis.

It has been my practice to consider the treatment of the jugular vein in three ways, depending upon the extent of the pathological process:

1. Those cases which have not shown symptoms of a general infection previous to operation, but in which a diseased sinus is discovered. The diseased walls of the vein are carefully dissected

away, the cavity gently irrigated and lightly packed for drainage. Nature here has most likely already limited the pathologial process by forming sterile, organized clots above and below. The jugular is not ligated, but the patient watched for symptoms of breaking-down of the clot and blood-stream infection. If such symptoms develop later, the jugular is ligated and the clot removed from the sinus.

2. The cases which have developed symptoms of acute septicemia or pyemia previous to operation. As soon as disease of the sinus is determined, the jugular is ligated at once to limit the infecting process.

3. The cases in class two in which, when the jugular is exposed, it is determined, by finding a clot in the vein or inflammatory adhesion surrounding the vein, that the pathological process has extended further. The vein is then dissected out to the lower limit in the neck.

When the vein is not diseased, simple ligature is preferable, because of the time saved and the small scar resulting in the neck. Beginning just below the region of the mastoid tip, a 2-inch incision is made, extending downward along the anterior border of the sterno-mastoid muscle. Through this incision the internal jugular vein is exposed by dry dissection, doubly ligated above the facial vein with chromicised catgut and divided between the ligatures.

Conclusions. 1. The surgical requirements in the treatment of sinus infections are (*a*) removal of the cause and (*b*) limiting the extension of the infection.

2. Free incision of the sinus wall is to be preferred when knowledge of its contents is desired.

3. Ligation of the internal jugular vein may be delayed when evidence of blood-stream infection is absent.

4. Surgical treatment of the jugular vein depends upon the extent of the pathological process, as determined by the symptoms and operative findings.

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## Agranulocytic Angina: Report of a Case with Fracture of the Tibia

ROBERT J. HUNTER, M.D.

In the last three years about a score of cases have been reported with the diagnosis of agranulocytic angina; agranulocytosis; leukemic condition with marked leucopenia; malignant leucopenia with low neutriphil count and similar titles. These cases have all had a peculiar blood picture, combined with lesions in the throat. As laryngologists we will be called to see these cases. It is for this reason that I present this subject tonight.

The onset is usually abrupt, with the symptoms of an acute infection, such as high fever, chill, headache, malaise, nausea, pain in the throat, teeth and bones. The cases have been in females, aged twenty-two to sixty-five years. As the disease progresses the throat becomes red and ulcerations, either single or multiple, appear. The tonsils are usually involved, and at times the cheeks, tongue, gums or larynx. There is a dirty-white fibrinous exudate upon the tonsil and surrounding affected areas, resembling diphtheria. This has been seen involving the superficial layers of the mucous membrane in some cases; but in some the tonsil was necrosed so that it looked as if it had been enucleated. In one case the tip of the tongue necrosed, as if about to separate, before death intervened. The odor of the breath is marked. Similar necrotic processes have been found in the vagina, intestinal tract and skin. A brawny induration of the skin of the left breast, and in our case an erythema multiforme, have been noted. The authors stress the fact that there is no tendency to hemorrhage into the skin; but in one case, which corresponded with this picture in other respects, there were petechia. Icterus has been seen frequently.

The blood-findings are the characteristic diagnostic feature. The red blood cells, hemoglobin and blood platelets are normal or slightly reduced. The white blood cells are markedly reduced, to as low as 600. The polymorphonuclear leukocytes are greatly reduced or even absent, thus giving us the name, agranulocytosis. The lymphocytes and large lymphocytes are relatively increased, to as much as 100 per cent (actually diminished, on account of the low white count). Transitionals are about 4 per cent. In some

of these cases, due to the difficulty in finding them, less than 100 cells were counted in making the differential. The bone-marrow shows a distinct decrease in white cells, with few or no granulocytes or myelocytes and many lymphocytes. The erythroblasts and erythrocytes are in normal number.

The Wassermann is negative; blood-culture usually negative, but the streptococcus hemolyticus and the bacillus pyocyaneus have been found. The latter was found in the throat and spleen after death in two cases. The coagulation time and the bleeding time are normal. Cultures from the throat have been negative for diphtheria and have shown the usual flora. Smears have been negative for Vincent's organisms, with but one exception. The urine has shown hyaline and granular casts, but no leucin or tyrosin.

Further general examination of the patient reveals no characteristic findings. Leon reports 3 cases with some enlargement of the spleen and liver and 3 without. The glandular system is not involved. The temperature range is 103° to 105° F. The course is from three to fourteen days and is usually fatal. One case has recovered and one has had a fatal recurrence in two years. Death has usually resulted from pneumonia.[1, 2]

Report of a Case. On May 10, 1925, K. F., a married woman, aged forty-five years, was admitted to the surgical ward of the Philadelphia General Hospital. The patient stated that on May 8 she tripped, fell and hit her left knee.

*Past Medical History.* She had milkleg eighteen years before, followed by varicose veins. Two years before, these broke down. She came to this hospital with bloodpoisoning of the leg. The leg was incised. She stated that she had had epilepsy since childhood.

*Sex History.* Married at nineteen years. Five pregnancies; no still births or miscarriages. Menopause, seven years before with no trouble. Removal of one ovary and suspension of uterus, twenty-three years before. Married twice. She has lived with present husband twenty-four years.

*Physical Examination.* The patient was a middle-aged, rather obese, adult female, lying in bed with complaint of pain in the left leg. Head, negative. Mouth and throat, strong odor of alcohol, otherwise negative. The tongue protruded in the midline, with some slight tremor at the tip. It was heavily coated. Both jaws were toothless. The nose and ears showed no apparent discharge or obstruction. The chest was of a large, obese, emphysematous type, with pendulous breasts. The percussion note was somewhat impaired at the right base, where scattered rales were heard. Otherwise the lungs were normal. The apex of the heart was in the fifth interspace, midclavicular line. There were no murmurs or thrills. The aortic and pulmonic second sounds were accentuated. The

abdomen was markedly pendulous. No pain or tenderness was elicited. The liver and spleen were neither palpated nor percussed beneath the costal margins. The inguinal glands were not palpable. The genital organs were not examined. The pulse was equal on both sides, easily collapsible; frequency, 100. The respiration was twenty-six; the temperature 99° F. The upper extremities were negative. The biceps reflex was normal. The right leg showed a normal knee-jerk, with no ankle clonus or Babinski. The left leg was markedly swollen from the toes to the hip. The left knee was very large, discolored and fluctuating, as if filled with fluid. Scars of previous incisions were seen.

*Provisional Diagnosis.* (1) Fracture of the left tibia. (2) Cellulitis of the left leg. (3) Epilepsy. (4) Acute and chronic alcoholism.

May 11 and 20. Urine negative.

May 11. White blood count, 5900 cells; hemoglobin, 9.6 gm.[4] polymorphonuclear leukocytes, 66 per cent; lymphocytes, 30 per cent; transitionals, 4 per cent. Wassermann negative to two antigens.

May 10 to May 20, the temperature averaged 99° F. with the highest 101° F.

Immediately before operation *x*-ray showed a badly comminuted fracture of the base of the tuberosity of the left tibia. This shaft of the bone had been impacted; another line of fracture went upward into the joint. The proximal end of the fibula was fractured.

May 12. An epileptic attack.

May 17. Buck's extension and Thomas splint applied.

May 20. Fracture set by Dr. Hearn, with nitrous oxide and ether anesthesia.

May 28. (Nurse's note.) Sleeps well; no complaint. At this point the temperature went to 102° F. for the first time and the patient complained of headache and pains all over the body. It became apparent that she was suddenly much worse.

May 30. A fine rash was seen on the chest and arms. It was thought to be a dermatitis, due to the intensely hot weather we were having at that time. This progressed in the next forty-eight hours to a typical case of erythema multiforme. There were no hemorrhages into the skin or mucous membranes nor any areas suggesting necrosis of the skin.

June 1. The patient complained of sore-throat, which rapidly grew worse.

June 5. The ears and nose were normal. The soft palate, uvula and the anterior pillars of both tonsils were eroded and red. The superficial layers of the mucous membrane were involved and the line of demarcation between the healthy and diseased mucous membrane was abrupt, without any surrounding area of erythema. There was no exudate. The tongue and the posterior wall of the pharynx were dry. There was some diffuse redness of the hard palate. Examination by Dr. Boston, the same day, revealed fine crackling rales at the end of inspiration, with some impairment on percussion at the base of the right lung, suggesting bronchopneumonia.

June 5. Blood count: Red cells, 3,200,000; hemoglobin, 8.1 gm. cubic centimeter; polymorphonuclear leukocytes, 0; lymphocytes, 89 per cent; large lymphocytes and transitionals, 5 per cent; unclassified, 2 per cent. A later count the same day showed white blood cells 1000; hemoglobin, 8.1

gm.; polymorphonuclear leukocytes, 0; lymphocytes, 93 per cent; large lymphocytes and transitionals, 5 per cent; unclassified, 2 per cent. A final count by Dr. Pons was white blood cells, 800; polymorphonuclears, 0; lymphocytes, 95 per cent; mononuclears, 5 per cent.

June 6. Blood culture was negative; there were no tuberuclar bacilli in the sputum; no Vincent's organisms in the smear from the throat. There were pneumococci, staphylococci and influenza in the throat culture; a heavy trace of albumin, a few hyaline and no granular casts in the urine.

After May 29 the temperature range was from 101° F. to 105° F.

The patient died on the evening of June 6. Permission for autopsy was refused.

Comment. This disease is apparently a distinct entity, although it has also been classed with the leukemias. It may be due to an acute infection. In sections of tissue vast numbers of bacteria have been found. This may be interpreted, however, as a result of the great reduction of polymorphonuclear leukocytes, rather than as a causative factor. Injection of guinea-pigs with bacillus pyocyaneus has indicated that this organism will cause a leukopenia, with a marked reduction in the percentage of neutrophils.

In our case the fracture and cellulitis may have been causative factors by opening the tissues to infection; on the other hand they may have been a coincidence. Seyderhelm[3] quotes Burger's case of acute hemolytic icterus following a fracture of the forearm. In this instance either the erythrocytes are destroyed more quickly than the marrow can supply them or the erythropoetic function of the marrow is depressed. In agranulocytosis a similar process is seen, except that the granulocytes are involved. In purpura hemorrhagica the platelets are diminished, and in aplastic anemia we have all the elements of the blood greatly reduced.

Cases of obscure ulceration of the throat, septic sore-throat and obstinate Vincent's angina should always have a complete blood-count taken.

Summary. Agranulocytic angina is characterized by ulceration of the throat and other organs, with a very low white blood count, showing few or no polymorphonuclear leukocytes.

The reported case was preceded by injury to the long bones.

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4. Multiply by 7 to get percentage.

## DISCUSSION

Dr. Edward Krumbhaar: This striking and clear cut clinical picture was described only three years ago by Schultze at a meeting of the Berlin Medical Society. The short account, which occupies less than a half a column in the *Deutsche Medizinische Wochenschrift* (1922, xlviii, 1495) covers, however, practically all the important points that have since been described. Dr. Hunter's case seems to be a fairly typical example. He considered the fracture to be a coincidence with the possibility of offering a site of entrance for the peculiarly virulent infection. One cannot say more, especially in the absence of a postmortem examination.

One of the still unsettled questions is whether the sepsis is primary or the change in the blood picture. A careful study of the cases hitherto reported make it clear that in some evidence of sepsis existed before the blood change was apparent, so that it seems much more likely that the sepsis is primary and the deficiency in the granulocytes (polymorphonuclears) results from the peculiar infection, just as it does in mustard gas, benzol poisoning and virulent influenza. Like these diseases, also, the fatal termination is due to a pneumonia, presumably so virulent because the leukocytic defense has been largely abolished.

In regard to the name, I would suggest that as the inflammation and ulceration are by no means confined to the throat, but have been found throughout the digestive tract and even in the vagina, "Agranulocytic angina" is less preferable than the more general term "agranulocytosis," or possibly accompanied by some limiting adjective such as "septic agranulocytosis." Just as in all blood conditions it is profitable to consider whether the lack of formed elements is due to decreased formation or excessive destruction or both, so in the present instance it is clear from an examination of the smears that there is almost total lack of formation of the polymorphonuclears. This is also confirmed by bone-marrow studies of the fatal cases.

It is quite remarkable, however, that inhibition of bone-marrow activity should be so strictly limited to the one type of cell. In most other bone-marrow dyscrasies such as pernicious anemia and purpura hemorrhagica, although one element may be diminished more than others, usually the others suffer as well to a lesser extent.

As these cases of agranulocytosis are presumably going to be recognized more often in the near future and perhaps most frequently by the nose and throat men, I think Dr. Hunter has done very well in bringing the condition to your attention.

## SPECIAL MEETING NOVEMBER 12

# Modern Methods in the Education of the Deaf Child

BY M. A. GOLDSTEIN, M.D.
ST. LOUIS

(By Invitation)

(*Abstract*)

Society's obligation to the deaf child is similar to that to the sick or crippled minor. In the past the weight of this obligation has not been sufficiently recognized, and, although progress has been made, the public still does not respond to the aid of this group of deficients as readily or intelligently as it does in making provision for the crippled or sick child. It is essential for the otologist to coöperate unselfishly with the teachers of the deaf. Too few otologists have accurate knowledge of the methods of training the deaf and the results that can be realized. Without this knowledge he cannot give the most valuable and accurate advice to the parent consulting him relative to the care and training of a deaf child.

Dr. Goldstein divided deaf children into two main groups: (*a*) The biologic congenitally deaf; (*b*) the pathologic congenitally deaf. In the former embryonic distortion or malformation of the hearing organs have occurred. This deafness is rarely complete and in 90 per cent of the cases the function of the static labyrinth is in part preserved.

Eight deaf children were presented to the society and the methods used by Dr. Goldstein and his teachers demonstrated. Of especial interest was the demonstration of the efforts made and the results obtained to secure tone perception and vocal-tone expression in the child not possessing enough hearing to differentiate sound elements. This was accomplished by tactile sensations originating in a sounding piano.

Dr. Goldstein emphasized the necessity of early training. The age of three is not too early. If education is too long postponed laryngeal atrophy and ankylosis makes vocal expression difficult or impossible. Discussion.

Dr. Packard asked Dr. Goldstein to tell of his experiences with radio devices.

Dr. Goldstein was of the opinion that such devices hold much promise but at the present time they are so much entangled by commercialism that there is great difficuty in obtaining accurate information regarding their efficiency.

Dr. Groover stated that the exhibition of the child taking a sentence by tactile sense from a megaphone was a remarkable demonstration by one totally deaf. If Dr. Goldstein could produce in groups results similar to this one produced singly much would be contributed toward the education of the deaf child.

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NOVEMBER 18

## Some Pharmacological Problems of Laryngology

DR. HORATIO C. WOOD, JR.

(*Abstract*)

Dr. Wood called attention to new grouping of silver compounds in the revised pharmacopœia. Those relatively low in silver content, about 8 per cent, of low specific gravity, and lighter in color being classified in the first group termed—Argentum Proteinum Fortus. The second group, Argentum Proteinum Mite, includes the thick, viscid, preparations containing approximately 20 per cent of silver. The protein silver combinations probably owe their germicidal superiority to a slow but continuous liberation of ionic silver.

Various local anesthetics were considered, and the two groups of toxic phenomena discussed, *i. e.*, (*a*) Convulsions, (*b*) syncope. In the treatment of syncope following the administration of a local anesthetic Dr. Wood considered adrenalin chloride intravenously and artificial respiration to be of great importance and value. Pituitary products, too, are efficacious. Attention was called to the fact that the speed of injection is an important factor. As a rule the slower the injection the less the danger of poisoning.

Benzocain, a comparatively new nonwater soluable local anesthetic, was mentioned. This preparation has very little toxic action and is of especial value when used as a dusting powerd in ulcerative throat conditions.

Discussion.—Dr. George Fetterolf asked the opinion of Dr. Wood as to the best antiseptic for small circumscribed skin infections such as aural furuncles.

Dr. James A. Babbitt requested further information concerning the action of a local anesthetic combined with adrenalin solution.

Dr. Wood said that tincture of iodine applied to the skin would penetrate deeply and disinfect a furuncle probably better than any other surface application. A saturated alcoholic solution of menthol has been used with success by some physicians.

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DECEMBER 16

## Some Complications* of Ear, Nose and Throat Diseases and Operations; Their Management

BY JOSEPH C. BECK, M.D.
CHICAGO.
(By Invitation.)

Preventive medicine, I believe, stands at the top today in so far as it promises to do the most good for the individual, since anyone would rather avoid being sick than being cured, no matter how slight the illness or striking the cure. The recently founded *Gorgas Memorial,* but already well advanced in its organization and activities, is going to do much toward the advancement of preventive medicine.

Prevention of complications both of diseases and operations, especially in my own field, is my hope and conviction, so that in ten years from now the presentation of such a topic as this before

* In the use of the term "complications," I do not wish to imply medical complications only, but those social, ethical and economic ones as well. The term "complex" is used in several instances with the same point of view in mind.

a medical body will be very rare indeed. Many complications frequently attendant upon ear, nose and throat diseases and operations are preventable with a thorough knowledge of the anatomy, pathology and technic of the operations. But by far the most important point in the prevention of complications resultant from disease as well as operations is the recognition of the early symptoms of a threatened complication.

The location of most of the special senses about the nose, throat and ear makes the earlier recognition of many complications easier. Most of those attendant upon the nose and ear develop intracranially, and that fact makes it incumbent upon the otolaryngologist to be a fair neurologist. In fact, to be able to manage complications of the nose, throat and ear, one must have a very good knowledge of general medicine or, better still, be a pluro-specialist. Of greatest value, at least to me, has been experience both in time and amount of material. Again, a physician who wishes to make a correct diagnosis of a threatening or existing complication of nose, throat and ear conditions should also be able to take care of the same, so far as it is within his field of activity, for much may be learned in the management of one case which is of value for similar cases in the future.

It will be possible for me to discuss only a few of the complications observed in my experience, since the time limit for this paper will not permit any great number; but I trust that I have chosen wisely so as to interest as many as possible.

Boils of the External Nose (Furunculosis). A teacher of mine at one time told me that "a boil, especially about the head and neck, has made up its mind at the time it first appears, just how large it is going to be and how long it is going to last before it opens or is ready to be opened. Therefore any effort to shorten its course may prolong it or cause trouble." This statement has positively proven to be true in my experience with boils about the nose.

Too-early incision, manipulations such as squeezing, etc., have led to a great many serious septic infections with occasional fatalities. The most frequent complication is a septic phlebitis, cavernous or great longitudinal sinus thrombosis. A chill in connection with a boil in the nose, no matter how slight, should be looked upon as a warning sign of sepsis. The blood picture will usually show the marked increase of leukocytes. The persistent headache, as a rule,

develops earlier than the edema of the lids. Locally about the boil one will observe the edema extending to the interior of the nose and the tip of the nose is more angry red or bluish-red in appearance. The regional glands of the neck are enlarged and tender to the touch. The general symptoms of high temperature and increased pulse-rate are of a decided septic character. The prognosis is extremely grave.

*Treatment.* The treatment consists in keeping the parts from being irritated; no active treatment or operation is advised. Bland ointments or lotions to the nose externally and intravestibularly are very gratifying to the patient. Three different substances at three different periods of my practice (several years apart) have proven themselves very satisfactory in the systemic treatment of this complication. First, in 1899, I employed antistreptococcic serum in combination with Hiss leukocytic extract intravenously. Second, in 1903, I employed blood transfusion, and in 1924 mercurochrome solution was used intravenously. All 3 cases recovered with a very stormy and long course of after-treatment, especially since additional complications or sequelæ, such as secondary anemia and persistent casts in the urine, developed. From the good result of these 3 cases one should not, perhaps, look upon this complication as of such grave prognosis as I have stated above; but I have seen other similar cases terminate fatally in spite of everything that could be done. I must say, however, that these were seen much later in the course of the sepsis. The causes of these fatalities were sepsis through the blood stream and lymph stream, and in 1 case a cavernous sinus thrombosis developed.

Emphysema and Sepsis following Fracture of the Nose. In former years fracture of the external nose following a brawl in a saloon was common in the receiving wards of our public hospitals, but now the automobile accidents have taken their places, far surpassing their numbers. Of course, the associated injuries of other portions of the face or the rest of the body are greater than a broken nose following a fight or any other usual attack on an individual. Fractures of the nose may also occur following intranasal operation, that is, if we consider the nasal accessory sinuses as part of the nose. This complication of fracture of the orbital plate, etc., we will consider in connection with complications of sinus disease or operations.

Nasal fractures are often compound and therefore apt to become infected. Frequently, in order to minimize the deformity for cosmetic reasons, the surgeon errs by neglecting to care for drainage and escape of air when the patient blows his nose. The organisms most frequently accompanying such injuries are the streptococcus and the tetanus bacillus. Erysipelas is not at all uncommon in connection with injuries about the external nose.

In any doubtful case of fracture of the nose the *x*-ray is usually to be depended upon. Both bone and air crepitus may be elicited in some cases.

The prevention of the complications lies in thoroughly disinfecting the nose externally before putting in splints and strappings. Small rubber drainage-tubes or silkworm-gut drains inserted at various points is a good practice. Avoidance of blowing the nose forcibly should be insisted upon and the patient advised to rasp the secretions back by way of the throat. Antitetanic serum should be administered in every case, especially if the injury has been caused by some old implement, etc.

General sepsis, which is probably streptococcic in origin and is demonstrated by blood culture, should receive the same treatment that has been described in connection with boils of the nose.

The supportive treatment of the patient, such as diet, rest, etc., must have the physician's closest attention, so as to prevent further complications of the vital organs, such as the kidneys, heart, etc.

Cosmetic "Pestiferousness." In recent years many rhinologists have been quite active in the correction of nasal deformities of the minor or cosmetic type and I have had the disagreeable experience of seeing quite a number of complications from these operations, my own as well as others. But the worst complications I have seen from this type of work were those from the hands of the quack and semiquack. This semiquack is the more dangerous and unfortunate since, in the majority of instances, he is a regularly licensed physician who has gone off on a tangent. Since the World War the public in small as well as large cities has gone mad on this cosmetic stuff, due to the publication in the lay journals of the wonderful accomplishments plastic surgery has attained through the misfortunes of the wounded soldier. In some instances our better-recognized men have published articles for the lay press encouraging cosmetic plastics. All such propaganda has been misleading and caused much misery. I do not deny the privilege of any

individual to change or have changed his or her features, but in the majority of cases after the attempt of correction, and I say "attempt" advisedly, these same individuals are not permanently satisfied with results obtained. In other words, these are the vain, self-centered neurotics and in reality should be treated for their mental instability. It is also true, as Dr. Vilray P. Blair puts it, that the psychology of these individuals must be taken into consideration, for in some cases one will find that an individual mentally depressed previous to operation becomes very happy after correction is attempted or accomplished. However, this type of individual is rare—and that is the *complication.*

All sorts of deformities are complained of, but the hump and the depression, or saddle, are in the majority. The large tip, the very wide nostrils, the twisted and double-twisted nose, wide bridge and collapsed nostrils make up some of the remainder of these so-called minor nasal deformities, some of traumatic but mostly developmental origin. All of these make valid reasons for correction, but these are not the ones mentioned before as neurotics who have little or no developmental deformity. The most common complication in this work is *infection* usually brought about by the operation from within the nose (vestibule) without sufficient attention to the preparation of the field and contamination from the interior of the nose. Seldom is this infection of a grave consequence or even severe. However, in the presence of an implant, it is further complicated by lasting either until the implant is removed or the cartilage becomes disintegrated or absorbed. I have seen several cases of fistulæ developed externally when the implant was introduced intravestibularly.

Cellulitis, Periostitis, Chondritis, Perichondritis. These are next in frequency and not uncommonly there is a *hematoma* present in these swellings about a corrected nose. *Hemorrhage* as a complication is not common, although bleeding of slow nature and difficult of control is frequent. I have been compelled in some instances to pack the dissected cavity with gauze for a period of twenty-four hours before going on with the operation, and one writer (Lewis) actually advocates this as a routine in implantation cases.

*Cellulitis* is of little or no permanent consequence unless it breaks down and forms an abscess.

*Osteoperiostitis* (usual) is of no consequence, but in some infected cases I have seen this reaction to be greater than the original deformity and the nose had to be reoperated. The sequestra formations may also occur occasionally.

*Perichondritis and chondritis* are the most important complications of those just mentioned. The perichondrium reacts so much as to produce an enormous, thick and stiff nose which, in spite of all efforts at reduction, remains permanently enlarged. However, the horrible thing is the chondritis when associated with infection, breaking down and causing a collapse and shrivelling of the greater part of the tip of the nose. Especially is this true in the various slicing or reducing operations on the cartilaginous portions of the nose. Fortunately, this complication arises but seldom and its infrequent occurrence is a mystery to me, but perhaps is due to the splendid circulation which, as has been pointed out by the earliest of writers, is the reason why we have so little trouble from operations on the nasal septum.

The management of complications just pointed out is really a matter of individual opinion. I have seen good men immediately open the wound when they find an infection about such an operated nose and permit drainage. Others pay little or no attention to it, but wait until either systemic, regional or tension symptoms are present. The latter method is my advice and practice. However, if an implant has been used and becomes infected, it is better not to wait too long, certainly not until an external fistula is threatened or formed, before removing such an implant. In cases of persistent osteoperiostitis and perichondritis causing marked swelling, the use of the electric-bulb heating lamps, mild massage, gentle but persistent pressure (from one-half to one hour daily), will aid in the reduction of this swelling. A nose that has shriveled from a severe form of chondritis must be reconstructed by implantation of either fat, fascia lata, cartilage or perhaps inlays of ivory; in years gone by, one might have said paraffin. This brings me to interpolating a brief statement concerning the complications of improper technic in the use of paraffin. I am one of the few left who has used paraffin for cosmetic surgery quite extensively without a single mishap or complication. I have, however, had quite a number of cases of these complications from other men, and one of these extreme cases I have illustrated and shown on several occasions. I believe the complications from paraffin

injections, such as a growing tumor or necrosis, telangiectasis, neuritis (both of the sensory nerve and optic) and other minor difficulties, are due to faulty technic. But why waste words and time, for we have no more use for paraffin in correction of nasal deformities? It must be said, however, that for minute fillings there is nothing at hand that takes the place of paraffin. Nevertheless, it should not be used, because of the danger involved in an individual's own special reaction to foreign bodies. In some instances he may be sensitive to paraffin, with the result that a paraffinoma—a very serious complication—may develop.

Another complication from faulty technic is overcorrection by implants. This is especially true in bone and cartilage, since they are more difficult in shaping in contradistinction to ivory. From such overcorrections, aside from the resultant ugliness, one may have a necrosis of the overlying skin, especially if the dressing be delayed more than twenty-four hours.

Major Plastic Surgery. Another type of plastic surgery which is somewhat a borderline field of the otorhinolaryngologist, oral and general surgeon is that of reconstruction plastic; in other words, true plastic surgery. There are nothing but complications in connection with thistype of work, and the meeting of them intelligently and promptly taxes the ingenuity of the surgeon.

There is one complication, however, that rarely if ever occurs, in contrast to those of minor cosmetic surgery already mentioned, and that is the dissatisfied, unsatisfied or pestiferous patient. Patients requiring reconstructive plastic work are the most gratifying individuals. Whatever is done for them is much appreciated and they quickly realize the impossibility of cosmetic reconstruction to their former selves.

*Major Plastics about the Nose.* The reconstructive work depends principally in obtaining tissues from other parts of the body, such as the face, forehead, arm or forearm, by way of pedicle flap-formation or direct, as Thiersch, Wolf and other grafts.

Necrosis of the flap or graft is the first complication always feared, and to the inexperienced many appear sure to die; whereas, the deceptive appearance is due only to the choking-up of the blood and the beginning of a reëstablishment of circulation. The less scar tissue present in the flap and area of union the less likelihood there is of necrosis of the flap. It stands to reason that asepsis, so far as is possible, has a marked influence on the life of the flap

and insurance of union. However, the marked tension and excess of twisting of the pedicles, the overdoing of the number of sutures, their coarseness and too-firm tying will frequently defeat a good operation by causing a necrosis of a flap or at least the edges. These complications are far more important than infection, which is, as a rule, of a mild character and union occurs in spite of it. In regard to the direct transplants of Thiersch, Wolf and others, death of them is the severest complication and in spite of the best technic will occur in more than one-fourth of the cases. Since the adoption of the Esser method of implantation of a foreign-body plug, to hold the graft down, results have been much better. Shrivelling up of grafts is the next complication and is quite frequent.

The occurrence of keloids in plastic surgery is one of the most discouraging facts in the work, since we have no knowledge before operation of this tendency, unless the patient has had cuts previously that formed keloid. In skin-grafting I have seen the donor's area develop marked keloids. In two cases wherein this occurred we were able to cause them to become flattened out by the use of radium.

Shrinkage of the flaps occasionally complicates a case of rhinoplasty, especially if the surgeon does not allow for it by making the flaps larger than the defect to be covered. The opposite is, however, much more frequently the complication, since there is an excess of tissue present. This complication is not so troublesome, because it permits of correction.

Hair-growth and different color and consistency of the flap are also seen at times and are very disagreeable, especially the hair-growth. This latter condition can only be eradicated by means of electrolysis, which in a large area is a Herculean proposition. This hair-growth, as well as the difference in color and consistency of the flaps, is obviated by the proper selection of the flaps and grafts.

Sinus Disease Complications. It is uncommon to see an acute sinus disease in adults complicated when these attacks occur infrequently and if they are not meddled with by local or mechanical means. In children, however, complications are not so rare. In these the periorbital inflammation from an ethmoidal or antral retention is characterized by an edema of the eyelids, even a chemosis of the conjunctivæ. The nasal examination usually reveals a marked swelling blocking the corresponding side of the nose. The general symptoms of high temperature and rapid pulse are

always present. While the ethmoid cells and antra are usually the seat of the trouble, the frontal sinuses and sphenoid sinuses are not exempt, except that in childhood these cavities are not as well developed as a rule as they are in the adult. In adults complications of sinus disease *per se* are usually in an acute exacerbation of chronic suppurative condition of the sinuses from extension through necrotic or fistulous tracts. Periorbital cellulitis, with or without panophthalmitis, is perhaps the most frequent complication. The eyelids (either upper, lower or both) become edematous and the corresponding conjunctiva is injected. Chemosis is usually present. As the process progresses, the eye movements become limited and at times painful; eventually a full-fledged panophthalmitis results. The process may be of a much milder character and produce an optic-nerve irritation or a retrobulbar neuritis which, when the nerve really swells, is associated with grave disturbance of vision.

There are forms of chronic sinus disease of a nonsuppurative character which can and do produce rapid loss of sight. The exact *modus operandi* of how this occurs has not yet been proven; but the characteristic enlargement of the blind spot with positive and relative scotomata presupposes a diagnosis of retrobulbar neuritis, and the exenteration of the posterior ethmoid cells and opening of the sphenoid have in a large percentage of these cases promptly restored the vision and dissipated other symptoms. In one of my cases of acute exacerbation of a chronic suppurative sinusitis I made a positive diagnosis of a choked disk, which disappeared after intranasal and external orbital operation. It has been stated positively by Cushing and others that a choked disk always means an intracranial increase of pressure. This patient had no symptoms of such condition and the spinal puncture was entirely normal both cytologically and as to pressure.

Complications from mechanical or surgical intervention in sinus disease are far more common, especially toward the orbit. In curettage of the ethmoidal labyrinth which happens to be necrotic it is very easy to enter the orbit through the periosteum. Depending upon the virulence of the organism present, a more or less virulent reaction occurs in the periorbital tissues, with all the concomitant signs. The infection may not limit itself to the orbital structures, but extend into the venous system, producing a cavernous sinus thrombosis, or may proceed along the optic nerve sheath to the meninges. In the latter event a meningitis of varying degree or

brain abscess may develop. A differential diagnosis between a panophthalmitis, retrobulbar cellulitis and thrombosis of the cavernous sinus may not be possible in these complications, since they may coexist in the same individual.

The next frequent complication of sinus disease, not by way of the orbit, is *meningitis*. This usually occurs by way of the olfactory nerves. This may be a local inflammation or a generalized affair, again depending upon the type of microörganism present, which will determine the course of such a complication. During the pandemic of influenza such as the world experienced during the later years of the World War, sinus disease complicated by meningitis was a diffuse type which very rapidly infected the brain tissue, causing death from encephalitis before the meningitides became apparent. In the ordinary type of influenza with sinus involvement the complication of meningitis is of a much slower development, rather a protective or serous type of meningitis. These cases do not terminate fatally, but often are recognized as lethargic forms of encephalitis. Meningitis from mechanical treatment of the sinuses, such as probing, etc., or following operation, is usually of the local forms of leptopachymeningitis. This need not occur by way of the olfactory area, but directly by extension from the frontal, ethmoid and sphenoidal sinuses.

The already existing head-pains of the sinus disease show a more continuous and constant character and usually the temperature and pulse become more significant. A spinal puncture will show an increased pressure: It may be cloudy or clear, the cellular contents are increased and it may contain pus cells with or without microorganisms.

The earliest focal symptoms of meningitis, aside from the headache, are the Kernig, Babinski and the knee-jerks, which should be positive. The pupils are sometimes somewhat sluggish and small or irregular, that is, one larger than the other. We cannot consider a stiff neck, drawn-up legs, dilated pupils, diarrhea or involuntary bowel movements and urination as valuable signs, since they are worthless, that is, they are antemortem symptoms. Vomiting is a sign to which I cannot subscribe much value. I have had a case of meningitis secondary to a sinus operation wherein severe photophobia was the earliest sign.

The next complication of importance in sinus disease is brain abscess. This is usually in the frontal area, although not neces-

sarily so, because the infection may travel along the surface of the brain and infect a distant portion of the same with an abscess, or it may go by way of the veins to a distant part of the brain.

Rhinogenic brain abscess is, however, prefrontal as a rule. There is usually a localized pain over the area of the abscess. The headache is at the site of the abscess, but it may be referred to any part of the head, spoken of as pain by contracoup. The pain and headache are much more excruciating than in meningitis and the sensorium is much clearer. This, however, will depend upon the degree of meningitis associated with the abscess. The spinal-puncture findings will be indefinite for the same reason, although the cell-count should not be changed very much. If the abscess be of considerable size, there should be a choked disk or at least a partial choke is present. Referring to the complication of *cavernous sinus thrombosis*, one will, of course, evaluate the source or origin of the infection, whether from the nose, sinuses, orbit, face or ears. The specific microörganism, if there be such, should be determined. The earliest sign of cavernous sinus thrombosis is due to the blockage of the return circulation. The eyelids are slightly edematous and the veins of the interior of the eye are distended. These two symptoms very rapidly increase, with considerable pain in the eyeball, and there is present congestion and edema of the orbital contents. The general symptoms of increased temperature and acceleration of pulse, with chills, complete the picture. Blood-cultures should be positive. The chills which recur so definitely in lateral sinus thrombosis are not so frequently encountered in cavernous sinus infection, at least so far as my observation is concerned.

The prognosis of a cavernous sinus thrombosis is very grave and until very recently no case (authentic) of a recovery from an operative procedure was recorded. Eagleton reported two cases operated and recovered. His procedure is to put the cavernous sinus at rest by ligating the internal carotid artery in the neck. He claims that the close proximity of the carotid artery to the cavernous sinus, by its constant pulsation, prevents the thrombotic process from becoming arrested or localized, as it does after ligating the artery.

The complication of retrobulbar or orbital pathological processes I shall not discuss, since they are of an opthalmological nature; but I do wish to state that these are both of distinct borderline conditions which may be handled either by the rhinologist or ophthalmologist.

Complications of the individual sinus are of special interest. The perforation of the frontal sinus externally, in the form of *osteoperiostitis abscess*, and subsequent fistula somewhere in the sinus region, are well recognized. This complication should never be permitted to occur, because there is plenty of time and signs to prevent the abscess formation, much less a fistula formation.

Common Colds. I do not here have reference to the local complications, such as sinus, middle-ear and mastoid disease, although in the true sense these are complications of the so-called *cold*. I refer rather to the extension to the lungs, heart, kidneys, etc., in the form of pleurisy and pneumonia, endo-, hyo-, myo- and pericarditis, as well as nephritis, arthritis, periarthritis and neuritis of all sorts. Of course, all these complications are within the domain of the internist and I am sure that I am not expected to elaborate upon them, yet I wish to make a definite statement in regard to the prevention of these complications by means of proper management of the acute process within the nose and throat. I am sure that it is not new to any of you, and yet I do know that it is the most neglected phase of the question. When a patient feels the prodromal symptoms of a head cold or a sore-throat or both coming on, the physician should know that any additional depressant will increase the virulence of the organisms, causing the acute process, thus reducing the fighting power of the leukocytes. In the majority of cases it is the chilling of the body that produces the depression. The next causative factor of depression is the overloaded gastrointestinal and urinary tract and lack of elimination both by the skin and intestinal tract. Finally, the imperfect ventilation of the upper respiratory tract is a third cause. From these premises one will apply the treatment: (1) By staying at home in a well-ventilated room and resting; (2) eliminating by skin, gastrointestinal tract and kidneys and taking of light but highly nutritious diet; (3) keeping the nasal chambers freely open by the mildest and nonirritating contractile remedies, such as a very weak solution of epinephrin. The most important thing to remember is that a patient with a cold should not be permitted to be active and become exposed to the chilling air, especially to the changing temperature, that is, going from a very warm room to the outer cold air and *vice versa*, as is the custom of our people in the cities.

The second important point to remember, and I am sure that I have observed this mistake made many times, is that mechanical

treatment of the nose and throat, such as nasal douches, sounds, swabs, etc., should be avoided during the height of the acute process. The commonest and most serious complication from any sort of treatment, during an acute nasal infection in which there are signs of blockage of the sinuses, is the use of a probe, especially in the frontal sinus, the result of which may be a meningitis or at least a local form of a brain abscess. In the case of a blockage of the antrum, it is the practice of most rhinologists to puncture the antrum through the inferior meatus or the natural opening and wash it out. There are some who believe in the use of compressed air to blow out the secretion. I consider this a very pernicious practice, as there are now enough cases of fatality and severe complications from this practice to warrant that statement. One very interesting and severe complication followed such a procedure in Chicago last winter.

In the case of acute throat infections the fatal mistake of operating on an acute, virulent *tonsillopharyngitis* is the most outspoken evidence of ignorance of pathology. The complication of such a procedure may be a septic endocarditis, a pneumonia or septic embolic diseases and infarctions. Locally, a most distressing neck cellulitis, or within the mouth a Ludwig's angina, may occur from such a mistake in treatment. Of course, the middle-ear infection with its whole train of complications is frequently observed when such a mistake is made; but much more severe is the complication following the cutting into of an acutely infected tonsil which is mistaken for a peritonsillar abscess.

Complications from a *peritonsillar abscess* itself are edema of the larynx threatening the life of the patient from suffocation; the rupture of the abscess and aspiration pneumonia; the sinking of the abscess anteriorly into the thyroid gland region, producing an acute thyroiditis or posteriorly into the neck and mediastinitis.

The management of complications from puncture of the antrum, air-douching and probing of the frontal sinuses is by prevention of the complications through avoidance of such measures. If one must puncture the antrum, it should be done through the inferior meatus and suction done through the trocar. If there be pus present, a mild irrigation is perfectly safe. As to the tonsillar complications, most of them are absolutely avoidable by doing no surgery beyond the opening of the peritonsillar abscess and that not earlier than when the presence of fluctuation is noted. If,

despite such precautions, complications do occur, expectant and supportive treatment are indicated except in the case of localized abscess or edema of larynx.

The complication is usually a general sepsis, and at the present time mercurochrome intravenously is the most popular means of treatment, although the actual results have not yet been compiled. So far as I am concerned, I am very much encouraged from the results obtained in the few cases that have come under my observation.

Chronic Tonsillar Infections. These are, of course, the whole group of diseases that are enumerated in chronic focal infections. However, there are a few that stand out more prominently and are more practical to discuss. Especially to be remembered are those structures that are lined with endothelial cells, for it appears that there is a predilection for these infections to lodge or develop on or in the endothelium.

In the first place, the entire vascular system, from the heart to the smallest capillaries; the lymphatic system of glands and ducts; the joints and bursæ; the nerve sheaths; the serous cavities, such as the peritoneum, pleura and pericardium; the dura mater and the whole cerebrospinal spaces, as the ventricles, canals and arachnoides are subject to infection.

Of course, infections from the tonsils do affect other than endothelial-lined structures, as, for instance, the renal epithelium, the end organs of the optic and auditory nerves, muscles, etc. All these, however, are the complications of chronic tonsillar and peritonsillar infection, particularly the latter. Let me make myself clear. It is very evident that tonsillar pathology, especially degenerated and retention crypts of the tonsils, produce local symptoms and systemic diseases; yet the majority of these crypts are open to the external world (mouth and throat) and are, therefore, not as likely to cause these severe systemic symptoms as, for instance, an apical tooth-infection or a closed-off ethmoidal cell.

With every attack of acute tonsillitis there is much evidence of peritonsillar inflammation and in some instances it actually breaks down to form an abscess. When the acute process subsides, the microörganism in the peritonsillar region settles down to the same production of slow infection and toxemia as from an apical tooth-infection. I will admit that very little, if any, research work has been done to prove what I have said; but, conversely, I have done some experimental work that proves the retention material within

the tonsil is not so much responsible for these general complications. I have taken a series of ten cases of typical chronic tonsillar infection with the various complications and subjected them to the most thorough tonsillar cleansing. First, I washed out all the crypts that I could see with normal saline solution; then employed mass suction and pressure of the tonsil; after which I passed a blunt-pointed cannula and sucked out each individual crypt. Subsequently, I injected into each crypt, by means of the same cannula, various solutions which are nonirritating, yet having bactericidal properties, such as neosilvol, mercurochrome, acriviolet, dichloramine-T., bismuth paste. In some instances, for control, one drug was used on one side and another on the opposite side. After waiting a sufficient length of time (one to four months) I found that while local irritation symptoms and the *fetor ex ore* were very much improved, the general or systemic condition was very little influenced. I then took three of these same cases and put my tonsillar ring-snare around the tonsil and everted it as if it were about to be removed. This was done to further insure the entire emptying of the crypts. The everted tonsil, looking like a cauliflower mass, was thoroughly painted with iodine and the snare taken off without removal of the tonsil. The primary result was "considerable reaction and a small hematoma in all cases, either in the posterior or anterior pillars." These, however, rapidly disappeared, yet the systemic general conditions were not influenced to any degree. What does that mean? It means that when the tonsil is removed with the capsule (fourth layer of the neck fascia) the peritonsillar infection is opened and properly obliterated. Therefore, complete or marked relief from general or systemic disease is obtained.

The treatment, therefore, of these complications *per se* is to prevent them by thoroughly removing the tonsils with the capsules intact. The remainder of any portion, no matter how small, may be productive of the continuation of these systemic difficulties, which I am pleased to call complications.

There may be such conditions of the system as to make the operation on the tonsil a greater risk than the condition demanding the operation, for instance, a very severe anemia as in the pernicious form, a severe leukemia, a markedly advanced diabetes or tuberculosis with much secondary infection, or a positive hemophiliac. Such cases, however, are not very common and some of them have

actually been risked and improved after operation, particularly the pernicious anemia and diabetes.

Complications from Tonsil Operation. These may be immediate, occurring on the operating table or later; between the end of the operation and complete recovery or even later.

While the *anesthetic* may not be considered as a part of the operation, yet it is one of the most important components of the surgical procedure and may complicate that procedure very much. The local anesthetic is the most favored, but not always applicable, as, for instance, in children and very nervous or apprehensive individuals. Fewer complications are, however, encountered from its use than that of the general anesthesia. Toxic symptoms are now more rare, since cocain is not injected as it formerly was before its substitutes, such as novocain and apothesin, were perfected. Topical applications of flaked cocain have given us the best results; but, for the past two years, we have been hesitant as to its use, owing to the ruling of the Committee on Anesthetics of the American Medical Association, which declared it not safe. I wish to state, however, that in the many cases wherein we employed it we had no trouble with it, and now since we use it less frequently we have considerable difficulty in sufficiently anesthetizing the area to do good work. Complications from the injection of the solutions of novocain or apothesin may be local or general infections; however, I have never seen or recognized this either in my own or consultation practice.

Complications from the general anesthetic are comparatively rare, since most of the standardized hospitals and surgeons employ only well-trained anesthetists and the preparation of the patient for the anesthetic is well carried out. In the use of the vaporizing apparatus one will at times observe a sudden slowing-up of respiration and a dilatation of the pupils. This is especially true in children, and, while most of these cases did not show any symptoms of thymic or lymphatic state before operation, we have examined them after operation and found an enlargement of the thymus shadow on the radiogram. Fortunately we have never had a fatality from such a condition; but the prompt recognition of these symptoms of slow breathing and dilated pupils, followed by immediate cessation of the anesthetic, has been responsible, I believe, for the good result. The suction tube (tip) is held close to the opening of the larynx, which aids in ridding the lungs of the ether vapor by a sort of pulmotor action.

For the past five years we have also employed another type of anesthesia, that is, an intermediary between a local and general, namely, "the synergistic analgesia." Complications from this type of anesthesia are supposed to be less. I cannot go into any detail about this form of anesthesia at this time, but will refer you to our publications on this subject, which appeared in the *American Journal of Surgery*, July, 1924, and *The Laryngoscope*, March, 1925. In the first instance it was published under the title of "Synergistic Analgesia as Employed in the First 1000 Cases about the Head and Neck." The later publication was entitled, "Further Report on Synergistic Analgesia as Employed in 3456 Cases about the Head and Neck." Let it suffice to say that there are complications, as, for instance, hematoma in the region of the injected morphin and magnesium; nausea and even vomiting at times occur, but this is comparatively rare. The results from this anesthetic are excellent.

A great deal might be said on the subject of *hemorrhage* in the tonsil operation; in fact, I might spend the entire time allotted me discussing that complication. I will, however, mention only the salient and my personal view-points. Aside from the real bleeder, diagnosis of which may be made from the history before the operation, one never knows whether he is going to have a severe bleeding during the operation. Neither the clotting nor the bleeding-time tests at all times determine this. The variations in the anatomical locations of the bloodvessels, their difference in size of the lumen and their pathological condition will determine that and only on the operating table. The technic employed, of course, has much to do with the question of bleeding, and I can positively say that in adults there is very little difference whether the tonsil is removed by a single instrument or is dissected. It appears that there is more bleeding when a single instrument is used, because all the cut bloodvessels are bleeding at the same time; whereas, in dissection when one vessel is severed it is grasped or compressed until the gland is out. Dull dissections are usually less bloody. The accurate grasping of a vessel, especially an artery, and positive ligation lessen the danger of hemorrhage and subsequent hematoma in the tonsillar fossa. However, in some cases sponge or clamp compression is necessary and is more wisely employed. Probably no other modern device has aided so much in stopping bleeding or preventing blood already spilled from entering the lungs or being swallowed as has the suction apparatus. Of course, it should not be used to

excess, thereby emptying the system of more of its blood than is necessary. Suction not only draws off the spilled blood, but secretions, as well as eventual vomitus.

A complication that is entirely avoidable by thorough examination of teeth, especially in children, is the breaking or *dislodging of loose teeth* by means of the mouth-gag and permitting these to drop into the throat. Cases are recorded wherein the tooth got into the bronchus or lung, causing lung abscess. The mouth-gag will at times *clamp the lips*, and if not discovered in time may so traumatize them as to produce a marked swelling, especially noted the day after operation.

Late Complications of Tonsillectomy. *Acidosis and Suppression of Urine.* The former is recognized by the odor of the breath, which, however, must not be mistaken for the paraldehyde odor in the synergistic cases and some odors from the saprophytic wound infection. Persistent vomiting usually accompanies the acidosis. The treatment of this condition is to rapidly alkalinize the system. However, there are authorities that claim that the use of sodium bicarbonate makes the condition worse and suggest the use of glucose and orange-juice instead. The suppression of urine is well recognized, and the proper treatment for this condition is to make use of other organs of elimination, as well as starting the action of the kidneys as soon as possible. Both of these complications are very serious and it is best to procure the aid of an internist in their management.

In all operations on the upper respiratory tracts and the oral cavity there is danger of *lung infection*, especially when a general anesthetic is employed, and from reports given, particularly by radiologists, one must admit that such infections are a common occurrence. I do not wish to appear as a braggart, but in all of my nose and throat experience I have seen but one case of lung abscess following an operation done under ether anesthesia. That was in a case of sarcoma of the nose. I think that this complication of lung abscess, or purulent bronchitis, can be avoided by the aid of the suction apparatus, bleeding being completely controlled either by ligation or clamping. It is the insufficient preparation of the patient before operation, overlooking at times the existence of an acute rhinitis, pharyngitis, tonsillitis or bronchitis, that leads to a lung abscess or a secondary purulent bronchitis. This is also true of a secondary pneumonia.

*Infection*, local as well as general sepsis, following a well-performed tonsillectomy in a properly prepared case is a comparative rarity. Infection of the tissues of the pharynx sufficient to be alarming has occurred in cases operated while acute inflammation and particularly virulent organisms, such as streptococci, were present in excess.

The marked edema without the tendency to pus formation is the most dangerous. The edema extends downward so as to involve the larynx, causing interference with normal respiration, in fact, may make intubation or, better, tranquil tracheotomy necessary. This condition of edema may be so severe as to make *swallowing* absolutely impossible, and, when attempted, retrojection through the nose occurs.

*Painful swallowing*, especially of fluids, due to the marked infiltration of the muscles of deglutition, is frequently an accompaniment of such severe processes.

Severe *cellulitis and lymphadenitis* of the neck and eventual abscess formation, simulating Ludwig's angina, is another complication. This may lead to great embarrassment in breathing and swallowing. *Thrombosis* of the veins in the region of the tonsillectomy and the neck is the rule in these cases, and the lungs and other regions of the body may become the seat of emboli and infarction, since the infection has entered the blood stream. This infection rapidly becomes diffused and the picture of a septicopyemia is the result.

In all these aforesaid conditions of infection the rapid pulse-rate and high temperature are very characteristic. The patient appears septic and the cytologic blood picture as well as the bacteriological findings in the blood stream are fairly constant. In other words, the diagnosis is only too clear and the prognosis very grave. Recently I had just such a case in consultation and, following the use of mercurochrome solution intravenously, the patient made a perfect recovery. Antistreptococcus serum has not proven very beneficial in my practice. Blood transfusion has, however, been of distinct benefit. Should the infection become localized and an abscess form in the neck, prompt opening and drainage is the proper treatment.

*Tubal, middle-ear and mastoid infections* are reported as fairly frequent complications to tonsillectomies. The *tubotympanic* symptoms are the most frequent, but seldom are they more than a transitory affair. Should, however, a tympanic complication result in which the drum membrane bulges and hearing becomes very bad,

it is best to incise the membrane at once. Mastoid and intracranial complications following tonsillectomy are notoriously of a more virulent character and are often protracted in the healing if operated upon.

*Sinus infection* as a complication to tonsillectomy does not occur so frequently as the reverse, namely, tonsillitis secondary to sinus infection. Appropriate care of the sinuses is, of course, the treatment; however, it is well not to manipulate the nasal mucous membrane in the presence of the infected throat any more than is absolutely necessary.

*Latent Abscess Formation within the Tonsillar Fossa.* Following ligatures of vessels, especially when silk is employed, the threads are either encapsulated or slough away with subsequent healing of the wound. In the event of abscess formation there will be noticed a persistence of a discharge with edematous or swollen pillars and pain on swallowing, probably due to the too-deeply-placed ligature. To cure the condition it is necessary to expose and remove the ligature.

*Perforation of Anterior Pillars and Destruction of the Pillars, including the Uvula.* In operations employing instruments whereby the tonsil is fed through the ring by means of the finger it is very easy, especially when the finger-nails are not properly trimmed, to perforate the anterior pillars. In the dissection operation it may occur that the posterior pillar is either severed with the tonsil or may be drawn into the snare with the tonsil and cut off. The same is true in the accidental removal of the uvula. Some of the anterior pillar may be removed by the blades of the guillotines in the Sluder operation. It is impossible to remove any of the pillar or the uvula if the ring snare is employed. Careful dissection of the tonsil before the snare is applied will avoid the cutting of the anterior or posterior pillars. Should the anterior pillar be accidentally perforated, it is best to do an immediate repair by means of a silk suture. The accidental uvulectomy will do no harm, provided that it is not so high as to take in any of the soft palate. If this later accident does occur, an immediate repair of the part is very essential, for in the absence of such repair the patient may have a nasal tone to his voice and, in swallowing, fluids may pass into the nose.

*Remains of Tonsillar Stumps (Inclusions of Tonsils) and Compensatory Lymphoid Masses.* Compensatory lymphoid masses

as a complication of tonsillectomy are by far the most important of these manifestations. Much trouble and dissatisfaction result from the inability of the next doctor who sees such a throat to recognize the condition and to make a statement or inference to the effect that a good operation has not been performed, whereas, in reality, it has been very well performed. The inclusion tonsil mass or other form of tonsil stump is, of course, a sad commentary on the operation and the acknowledgment of that fact is the best attitude to take toward the patient. In the case of masses developing at the inferior portion of the tonsillar fossa or the presence of compensatory tissue, especially of the plica triangularis, the problem is entirely different. One will find these very frequently in spite of the fact that a perfect operation has been performed, especially when the hypertrophic plica has been allowed to remain. Compensatory formation at the lateral parts of the base of the tongue, as well as the lingual tonsil itself, occurs in some individuals no matter how one deals with the operation. It, therefore, behooves one to be extremely careful in reference to criticism of the operation. Do these masses cause trouble? Indeed they may, and actual recurrent attacks of sore-throat are observed in these patients and an occasional general systemic manifestation may also be seen. It is necessary in such instances to do either a secondary operation or destroy these masses by some other means. The great difficulty is the associated oozing and the controlling of it in the lower pharyngeal region. It should always be followed by proper ligation of all bleeders and compression of the oozing surface.

In the last two years I have preferred to destroy these masses by means of electro-coagulation (surgical diathermia), thus avoiding the above-mentioned oozing and yet obtaining equally good end-results. Of course, in cases of inclusion tonsil masses and remains of true tonsil stumps, it is necessary to do a thorough re-removal of them and repair any damaged part of the pharynx.

*Atresia of the Soft Palate.* The adhesion of the soft palate to the posterior pharyngeal wall occurs in cases wherein the dissection operation is carelessly performed, thereby denuding surfaces of the soft palate, posterior pillars and the posterior pharyngeal wall. This is most likely to occur in a traumatizing adenoid and tonsil operation with lack of after-care while the parts are healing. The difficulty from this complication is *nasal obstruction* and a blocked, nasal voice. Once this atresia is formed and organized, it is neces-

sary to do quite an extensive plastic, which under the best of conditions often fails.

*Cicatrization and Deformity of the Soft Palate.* This is a very common complication, but not very often complained of by the patient. It is the ugly appearance of the throat that is objectionable. The cause is mostly a careless dissection, but it may be due to the marked reaction resulting from the operation, usually the dissection. It may also follow an infection following the operation. When the deformity is so great as to foreshorten the palate, the patient may develop a nasal voice, and in a few cases patients have complained of fluids going into the nose when swallowing. Some patients, particularly nervous individuals, complain, out of all proportion to the lesion produced, of the drawing feeling in the throat from the stiffened and scarred muscles of the palate. Burning sensations extending into the tongue are not infrequent. Tiring easily produced by speaking or singing, is an additional symptom. A dry feeling is also at times complained of.

The management of all these apparently inconsequential complications will tax the ingenuity of the physician, since most of these patients are neurotically inclined. I have found that injections of normal saline solutions, usually about fifteen to twenty drops, into these scars are of most value in the majority of these complaints. The injections are repeated two or three times. If the palate appears tightly drawn, introduction of the finger postpharyngeally once or twice a week appears to be effective.

*Delayed and Nonhealing* (undiagnosed systemic diseases previous to operation). Occasionally one will operate on a case in which the healing is very much delayed or where there is no tendency to heal, eventually unhealthy granulations springing up within the fossæ. On investigating, one may find that the patient has either active syphilis, tuberculosis, diabetes or some other constitutional disturbance. A differential diagnosis with the aid of the microscope and other laboratory tests may be necessary.

Appropriate treatment to general conditions does invariably bring about good results. I recall several such instances and one case of a nondiagnosed lymphosarcoma of both tonsils, previous to operation, was followed by very rapid sarcomatosis of the throat and neck, quickly killing the patient.

The *lingual tonsil* may be so hypertrophied as to cause symptoms and require removal. When using a sharp curet or a guillotine,

the subsequent bleeding may be so brisk as to resemble a hemorrhage. Grasping by artery clamps and placing one or two sutures will invariably stop it, but constant pressure with a flat applicator soaked in some astringent solution may be necessary. In one case a searing of the surface had to be done and in another a tracheotomy was necessary in order to pack the pharynx completely and firmly before the bleeding could be brought to a standstill. In one case, seen in consultation following operation, the epiglottis was firmly adherent to the base of the tongue, causing a constant cough.

Complications from Adenoid Disease and Operations. So large may be the adenoid mass as to completely block the Eustachian tubes and cause a pronounced reduction of hearing. In the newborn it may also cause inability of the infant to nurse sufficiently long, and exhaustion due to the fact that it is unable to breathe while nursing. The nasal accessory sinuses, as well as the middle ears, are constantly exposed to infections from the blockage to ventilation. Malignant disease, especially lymphosarcoma, may develop in an adenoid mass and be very rapidly destructive, especially if it extends toward the cranial cavity by way of the sphenoid bone and sella region. In the adult, in whom the adenoid mass has disappeared but there is still present the remains of the marked folding and pocket formations with retentions, we may have what is known as Thornwald's disease, or pseudobursitis. In tertiary syphilis we frequently have a gummatous breaking-down of the adenoid region, especially in the "hereditaria tarda" individuals in whom, after healing, marked cicatricial stenosis develops.

Following the usual adenoid operations no complications are observed, but the question is often asked as to whether the adenoids redevelop. *Marked granulation formation* may simulate such conditions, and on examination they have proven to be *tuberculosis* in several instances. Also in cases where, after operation, a secondary pus-infection results, granulation formation may follow.

*Hemorrhage.* At times very sharp and continuous bleeding persists after operation, which the little patients swallow, and if deeply enough anesthetized this may fill the bronchi and lungs, conditions that may further complicate the case.

Acute Laryngitis with Edema, Perichondritis or Abscess. In acute laryngitis, whether traumatic, infectious or from whatever cause, the edema is the most-feared complication. The rapidly

developing difficulty of respiration with the added anxiety form a picture that once experienced is not easily forgotten. Especially is this grave when there is present an external swelling about the larynx or neck, probably a perichondritis or abscess. The edema of toxic origin, or of chemical origin—such as sometimes follows the administration of potassium iodide or salvarsan—or the edema secondary to some cardiac or renal condition or even following trauma is not as serious because an intubation or a bronchoscopy will tide over the patient until the cause is removed. In edemas associated with foreign bodies, as soon as the *corpus alien* is removed, the swelling usually subsides rapidly, although a tracheotomy may have been necessary. When an abscess or perichondritis of the larynx is present, it is well to do an external operation, in order to relieve the venous bloc within the larynx as soon as possible. At times multiple punctures of the edematous mucous membrane afford immediate relief. Inhalations of steam, sprays and topical applications should always be tried, but not to the point of a threatened suffocation followed by the necessity of a hurried tracheotomy. It is much better to perform a tranquil tracheotomy and save the life of the patient, at least sparing excessive trauma.

Of course, the diphtheritic infection in preantitoxin and cultural period had the largest number of edemas of the larynx, but these are now comparatively rare. Should one have a case of this kind, a direct laryngeal exposure and the passing of a bronchoscope will often save the life of the patient. If a tracheotomy is necessary in such a case, the bronchoscope in place will give the surgeon time enough to do it slowly.

Foreign Bodies, with their Complications. There are quite a few complications associated with foreign bodies of the larynx (trachea) and their removal. One—edema—has already been referred to. Next in order is threatened suffocation from the foreign body itself, especially if it be large and wedged into the chink and transversely. Tracheotomy and immediate removal by pushing the foreign body upward is the best method of handling such a case.

*Infection* with perichondritis, suppuration and abscess formation, both externally and internally, are occasionally met with and require immediate and adequate treatment to prevent a later complication of cartilage absorption with collapse, or cicatrization and atresia with all their associated difficulties. External incision of abscess without cutting into the cartilage and good drainage is the treatment par excellence.

*Hemorrhage* following the lodgment of a sharp foreign body (one case from glass has been observed by me which required a tracheotomy to stop it before removal could be attempted) can usually be controlled by applying ice compresses externally and permitting the patient to swallow pieces of ice.

Pneumonia and Lung Abscess. It will suffice to say that these complications occur with less frequency in these times of direct laryngoscopic operations. Only if the case becomes further complicated by the dislodgment of the foreign body and passage deeper into the smaller bronchi, is pneumonia likely to develop. In that case it is not a "foreign body of the larynx," but of the bronchi.

The treatment of pneumonic and lung abscess is an extensive subject and principally a medical one, so far as the pneumonia is concerned. Lung abscess is being successfully treated by bronchoscopists, particularly in some of the special bronchoscopic clinics. In this manner the general or chest surgery has to take second place, because the prognosis is so much better when the lung abscess can be treated by means of the bronchoscope and suction in contradistinction to lobectomy, etc. Again, these major lung operations can always be performed after the bronchoscope fails.

Laryngeal Pemphigus. This should be considered a complication of a generalized pemphigus. It is a manifestation of blisters and a great deal of reaction about the epiglottis and arytenoids. There is much pain on attempting to swallow, so that the patient refuses food and says he would rather starve than eat or drink. Pemphigus is primarily a dermatological condition of great severity and grave prognosis. The etiology not being known, makes the treatment still more difficult; in fact, in our three cases it was useless. It is the skin involvement that usually appears first, which makes the diagnosis of the laryngeal condition easy; but in one of our cases I made the diagnosis of pemphigus from the laryngeal picture, since there was no skin lesion at that time. Where locally treated by mild and strong applications of a variety of remedies, no difference was discernible, and general treatment by arsenic preparations, mercurochrome and coagulose had apparently a beneficial influence, but the patients died despite that. Since the outcome is so universally fatal, it behooves one when confronted with this condition to employ heroic measures, especially toward the breathing and swallowing, and I have made up my mind that in any further cases

that may present themselves tracheotomy would be done, in order to put the larynx at rest as well as to make possible more efficient application of local treatment. I have further determined to pass either a permanent Rehfuss duodenal tube or have a gastric fistula made in order to stave off starvation.

Tubercular Laryngitis Complications. Tuberculous laryngitis is often complicated by the exaggeration of its symptoms of pain, especially on swallowing and obstruction to breathing. Both of these conditions call for surgical or semisurgical remedies. In the former difficulty the injection of the superior laryngeal nerve may give much relief, and in the latter a tracheotomy will relieve the distress. At a recent meeting of the American Laryngological, Rhinological and Otological Society, Dr. J. Dworetzky reported statistically from several large sanatoriums for tuberculosis and from his own experience, a large number of successes in the prevention and treatment of tubercular laryngitis. This was accomplished by artificial pneumothorax. He showed quite conclusively that in cases of tuberculosis of the lungs in which this procedure was done the laryngeal complications did not develop. He further showed that in cases wherein an active process of the larynx already existed it was arrested or minimized by pneumothorax.

*Tubercular perichondritis and abscess* are not common, but when they do occur they should be opened externally as early as possible to prevent absorption of the cartilages of the larynx. The ulcerative forms, such as heal out in scar formation either spontaneously or from treatment, may and do cause marked stenosis. The treatment of this complication will be discussed later in connection with all forms of stenosis of the larynx.

Luetic Laryngeal Complications. These may occur in consequence of administration of either K. I. or salvarsan. It is the edema or Herxheimer reaction heretofore mentioned in this paper. In the presence of luetic laryngitis the administration of these two drugs should always begin with small doses, and should excessive swelling of the mucous membrane appear and tend to remain, it is good practice to prevent a serious embarrassment to breathing by temporary tracheotomy. Since the active antiluetic treatment by salvarsan must be carried on also in order to cure the patient of the generalized disease, the practicality of such a tracheotomy is recognized, since the administration of salvarsan is followed by edema.

Gummatous formation and breaking-down to form an abscess is a very common course. This invariably produces a coagulation necrosis of the cartilages of the larynx, at least partial. Low tracheotomy should be done as soon as fluctuation can be made out and the abscess or broken-down gumma should be drained. There may be externally a sequestration and extrusion of particles of the cartilages, with danger of secondary collapse and deformity. This latter complication may be prevented by early external incision and very active antiluetic treatment. These deformities, should they occur in spite of the above treatment, will be described later in connection with all forms of stenosis.

Rhinoscleroma of the Larynx. This disease is rare in this country, having been imported from certain sections of Europe, as Russia, Roumania and various other countries. The process is found first in the nose and secondarily affects the larynx, without very much change in the pharynx. It has a chronic course and resembles either a tubercular or syphilitic process. The specific cause is the bacillus of Frisch.

The characteristic change is the narrowing of the lumen of the larynx, with corresponding dyspnea and loss of voice. Early tracheotomy frequently becomes necessary. The real complication is extension downward into the trachea and even into the bronchi. Cases are reported of the extension into the esophagus and stomach, but I have never observed such a complication. I have seen a case of rhinoscleroma of the nose wherein the condition was so extensive as to spread the bridge of the nose and cause ulceration externally. Whenever the extension tracheawards occurs to such an extent as to block both the bronchi, it becomes necessary to pass a bronchoscope into both right and left sides, and through the bronchoscope introduce a semistiff rubber; in other words, intubation of the bronchi is done to sustain life. I was obliged to do this procedure in the case of a girl, seventeen years of age, in whom there developed marked symptoms of respiratory embarrassment. The repeated passing of the bronchoscope kept the trachea patulous and finally the rubber tube could be left out permanently.

Potassium iodid internally and combined radium and *x*-ray treatment have been found to be of value in the treatment of this affection. Cicatricial stenosis, in event the process comes to a standstill, have to be operated and treated as will be described in a subsequent chapter.

Laryngeal Neoplastic Complications. These may be divided into malignant and benign forms.

One of the types of benign growths is the *fibroma* or *vocal nodule*. The one complication that may occur after the removal of the growth is marked change or loss of voice. Since the nodules occur most frequently in singers or speakers and their vocations may be of potential earning value, one will realize the importance of such a complication. Since the advent of the direct laryngoscopic method which is employed for the removal of these small excrescences, this complication has been very much minimized, especially when it is performed under synergistic analgesia. The operator is thus enabled to have the patient completely relaxed and the movement of the larynx markedly restricted.

In the case of larger growths, such as *fibromyxomas* of the larynx, the chances for such a complication are much less and the same procedures above mentioned will further insure safety and success.

*Papillomas* of the larynx are at times complicated by marked dyspnea, calling for a tracheotomy. This condition is more frequent in children, and the need of a general anesthetic in case of removal complicates the matter considerably, owing to the respiratory difficulty. Therefore, a preliminary tracheotomy is a safer procedure. In older individuals, of course, no anesthetic or only a local one is employed to pick off the papillomatous masses.

From the frequent removal of the ever-recurring growths there finally develops considerable scar formation, which may complicate the case by producing a stenosis and a marked change in the voice. The same is true when radium (either needles or seeds of radium emanations) is employed in the treatment of the papilloma. The cicatrices following its use, by incompetent men particularly, may be marked. The treatment of the complication of cicatrization will be discussed in connection with the complications of strictures of the larynx from any cause.

I have had a case of papilloma of the larynx complicated by extension of growth behind the tracheal cannula and externally about the tracheal opening, over the skin. In another case, either due to the excessive operations or the secondary infection, a great portion of the laryngeal cartilage became absorbed, so that the patient was doomed to have a permanent tracheotomy with little or no voice.

Of the *malignant growths* of the larynx, *carcinomas* are the most frequent. In fact, I have seen only one case of sarcoma and one of

endothelioma of the larynx in contradistinction to more than one hundred carcinomas.

Of the four cardinal symptoms of hoarseness, dyspnea, dysphagia and pain, the last three may be so great as to be noted as complications. The case may be further complicated by metastasis into the regional glands or extending into the esophagus by continuity of growth. Generalized metastasis also complicates the condition.

The dyspnea will call for a tracheotomy and the dysphagia for the use of a Rehfuss tube or a gastric fistula in order to sustain strength and prevent starvation. The pain usually necessitates the free use of narcotics or injection of the superior laryngeal nerve with alcohol. All three of these symptoms are relieved by operation and all four have been reported as having vanished (though not in our experience) by the aid of *x*-ray and radium treatment.

*Biopsy* may complicate the case in more ways than one. It is stated by some that, following the removal of a piece of tissue from the larynx for microscopic diagnosis, a more rapid spread of the disease occurs. Therefore, they say, that unless the patient gives his consent to have the operation performed in order to prove the specimen malignant, a biopsy should not be done. I am opposed to this statement, because I have not observed any greater activity following a well-performed biopsy, and, second, a biopsy is performed only in the major laryngeal procedures, as in laryngectomy. In the thyrotomy, or window resection, the microscopic diagnosis is made after the entire growth is removed. A biopsy may not always be infallible. I recall a case of fairly well-advanced carcinoma of the larynx wherein the report of biopsy was fibropapilloma. I, therefore, performed a thyrotomy and removed the growth as thoroughly as possible and again closed the larynx. The subsequent microscopic examination of the growth removed revealed a very active cell-growth of a carcinoma. This proved a great shock to the patient, particularly since a laryngectomy had to be immediately performed.

Operative procedures for the removal of a laryngeal growth may be considered in the following manner:

1. Intralaryngeal removal of growth by means of cold instruments or the electrocoagulation methods, either direct or indirect.

2. Laryngofissure: Splitting of the larynx, removal of the growth and immediate closure.

3. Window resection of the side of the thyroid cartilage occupied by the growth and removal of the growth.

4. Hemilaryngectomy: Removal of half of the larynx, including the growth.

5. Total laryngectomy.

Complications following Operative Procedure of Removal of Growth from the Larynx. Complications from this cause are not so frequent if preliminary trachectomy is performed. *Edema*, with difficulty in respiration, is the most frequent. *Lung* and *mediastinal* complications are less frequently observed. I have seen a *laryngo-esophageal fistula* follow the removal of the neoplasm by the electrocoagulation method. Following thyrotomy, and particularly window resection, considerable difficulty in swallowing may occur for several days after operation. Cellulitis and adenitis, as well as abscess formation, are occasional complications. Non-union of the laryngofissure may occur and suppuration continue for some time, with minute cartilage necrosis and its extrusion. Following hemilaryngectomy, lateral collapse may develop, so that when the tracheotomy tube is removed the patient may have great difficulty in breathing. In one case I was compelled to leave the tracheal cannula permanently in place. Complications following total laryngectomy are being gradually decreased by those who are devoting a great deal of time and effort to this operative technic, especially toward the proper preparation of the patient for operation. Of course, proper preparation applies to any operation, but especially to this major procedure. Such systemic conditions as diabetes, severe blood dyscrasias, as anemia or leukemia, cardiovascular disease, renal disease, lues and tuberculosis must always be reckoned with as possible factors in complicating the operation. The psychic state of the patient must be studied and all possible attention given to the phobias, particularly in regard to the *loss of the voice*. It is well to have the patient know that even though the whole larynx be removed he will be able to speak by means of a buccal, esophageal or even stomach voice, and also make use of the perfected artificial larynx of MacKenty. I have several patients who are using this instrument with gratifying results. I also have prepared phonographic records of patients speaking after laryngectomy, both by aid of the artificial larynx as well as the buccal, etc., voice.

The properly chosen and properly administered anesthetic, too,

has decreased the number of complications, especially the pneumonias, lung abscesses and mediastinites. We have in recent years employed the synergistic analgesia in combination with local infiltration of the operative field. This has given excellent results (*American Journal of Surgery*, July, 1924, and *The Laryngoscope*, March, 1925).

*Neck abscess and necrosis or sloughing* are not often seen since proper drainage of the areas of the dissected larynx pockets was instituted.

The sustenance of the patient's strength by means of the feeding through the Rehfuss tube, which remains in position for several (five to seven) weeks, that is, until the neck wound and esophagus are closed, is of prime importance in preventing symptoms of inanition.

In conclusion, I wish to state that the use of the *suction tube* to remove the secretions from the trachea and bronchi, especially immediately after operation, thus relieving the patient from constant desire to cough, is one of the greatest modern adjuncts in preventing several of the complications, and aids in the more rapid healing.

I also wish to state that a competent nurse—in fact, two for the first two or three weeks—preferably those who have had experience and training in taking care of the laryngectomy cases—has much to do in preventing many of the complications and giving them proper care should they occur.

The various complications that have been mentioned in connection with the different operations on the larynx, in connection with malignant disease, are met with in the usual rational methods as outlined in reference to other laryngeal disease and need not be again repeated.

*Stenosis.* As already referred to, in the various pathologic conditions of the larynx and trachea, the ultimate or terminal stage is *cicatricial* stenosis. It makes considerable difference as to what the particular process is (for example, post-tubercular, luetic or after a radium burn), for the cicatrix varies in its density, depth and distribution. As a general proposition, however, there are but three rational remedial measures to relieve the one great difficulty, namely, breathing.

1. *Tracheotomy*, if it has not already been performed during the activity of the disease, may be the only possible procedure. Although

the voice is more or less lost, unless the patient blocks the external portion of the tube, the subject is very much gratified by the relief of air-hunger. There are tracheotomy tubes now manufactured that close by means of a valve and which do not require the use of the finger every time the patient wishes to speak. The technic of permanent tracheotomy should be carried out tranquilly and one should be sure that he is below the cicatrix. Of course that may require special forms and sizes of tubes when the stenosis is in the trachea.

2. *Dilatation* by means of sounds (bougienage, intubations, etc.) is of value, particularly the electroheated bougie. Whereas radium may produce burns which terminate in cicatricial stenosis, radium itself is employed as a therapeutic measure to soften the scars and enable the bougie to dilate the strictures. Stenosis from web-formation is best corrected by first excising or punching out the part of the web and following shortly after with bouginage. Other adjuvants, such as the use of scar solvents (for example, fibrolysin, thiosinamin), may be tried, but I personally have never seen much benefit from them.

3. *Laryngostomy* must be performed in all cases not suitable for dilation; that is, in extreme cases of cicatricial stenosis. The results from this operative procedure have been quite satisfactory in my practice in so far as restoration of a good breathway is concerned, but the voice is seldom very good after the operation. In cases of extreme laryngeal stenosis, wherein a great deal of the cartilage of the larynx has been destroyed or become absorbed, a laryngostomy is impossible and only a permanent tracheotomy is indicated. In order that such an individual may speak, he must use either a buccal or pharyngeal voice, or else employ the artificial larynx as do the laryngectomized patients.

Complications of External-ear Disease. The external-ear diseases most commonly met which are capable of producing complications are:

1. *Othematoma and "Puge" Ears.* These may become infected, with a resultant perichondritis and subsequent shrivelling, known as "cauliflower ear," or a stiffening both as to appearance and feeling, the so-called "tin ear." Avoidance of infection when turning out the clot and proper adaptation of the parts after this has been done may prevent these complications. When the perichondritis with abscess is established, free opening, drainage and readaptation

of the raised skin is the best treatment to avoid the shrivelling of the pinna. The shrivelled ear itself must be reconstructed by means of plastic operations, such as inlays of ivory, cartilage or bone. This should, however, never be done before all signs of infection have disappeared. The stiff or so-called "tin ear" can be but very little influenced by treatment. However, massage and heat applied by the aid of an electric-light bulb may be of some benefit.

2. *Frost-bite.* After an ear has been frost-bitten once it is easily bitten again and a perichondritis with deformity usually follows; therefore, to prevent this complication, the ears should be protected in cold weather by wearing ear-muffs. In case of the frost-bite taking on a more serious aspect, such as serous effusion, this is drawn off early with the strictest aseptic precautions. Ichthyol and vaselin is the best local application. The deformity must be attended to in the same manner as that following perichondritis and abscess from any other cause.

3. *Burns.* Deformity and destruction from actual fire is the severest form of burn. The degree of destruction, of course, varies in each case and consequently the treatment is likewise individual to a marked extent. Antiseptic dressings and the old limewater and linseed oil applications are the best remedies to minimize the loss of tissue and the best for relief of pain. Burns from radium and *x*-ray are entirely avoidable; but since these remedial agents are very much used, and many times by men either incompetent or poorly trained in the use of such agents, complications very frequently occur. Some of the resultant complications are telangiectasis, marked cicatricial formations and even destruction of parts Treatment is the same as employed for other burns, but it must be remembered that healing is much slower. Chemical burns, as from acids and alkalies, may be either accidental or intentional. The prevention of complications due to destruction and subsequent cicatrization lies in immediate attention to the burn by neutralizing the chemical as quickly as possible. Washes of neutralizing reaction are employed, and lotions or salves of the same are used, always in excess in quantity to insure neutralization. After that, the use of bland ointments and lotions is indicated.

To correct these destructions, contractions and malformations following burns, great patience and ingenuity are required. However, one can mention the electroheated bougie as of distinct value in stretching scars and opening up the external auditory canal.

4. *Trauma of the External Ear.* These vary a great deal and so may the complications. The most important fact to remember is that some wounds may lead to tetanus, therefore antitetanic serum must be used to prevent it. Injuries to the canal carry with them the possibilities of stricture of varying degree. To prevent this one will keep the raw surfaces apart by means of rubber tubes and packing. Some of the slightest traumas, especially of the external auditory canal, have led to severe complications whenever a severe infection intervened. This has been especially observed in efforts to remove wax or other foreign body. It has also been noted in individuals who have the bad habit of scratching their ears with all sorts of infected implements, such as toothpicks, matches, hairpins, pencils and the special ear-spoons. Most cases of furunculosis, erysipelas and some eczemas are due to this cause. This is particularly favored by the presence of the Bacillus pyocyaneus, whose normal habitat is the external ear.

The major traumas of the external ear, especially those produced by automobile accidents and war injuries, require much time and space for discussion, not possible in such a paper as this, and since each case is marked by individual characteristics, no generalization other than that already mentioned can be made.

5. *Erysipelas* is an infection constantly feared as a complication to injuries about the external ear, almost as frequently as about the vestibule of the nose. The diagnosis is not difficult, but such conditions as a dermatitis from chemicals, especially iodoform or iodin, and some forms of acute eczema must be differentiated particularly on account of the danger of spreading the contagion in erysipelas.

6. *Perichondritis* from any cause may be complicated by coagulation necrosis, abscess formation or shrivelling. Prompt relief of the abscess by the use of moist dressings and ichthyol-vaseline dressings will frequently prevent the complication of shrivelling of the ear.

In perichondritis of the external canal there may follow a perforation into the soft tissues of the neck below and in front of the mastoid or posteriorly, to simulate a mastoiditis. As a late manifestation there may develop a marked constriction of the canal, which in the presence of a middle-ear suppuration further complicates the case by retention in the middle ear.

7. *Eczema* may become complicated by secondary infections due to scratching of the intensely itching surfaces. Thus an inflam-

mation of the canal is not at all infrequently seen. Prevention of scratching is most important in the treatment. The diffuse swelling is best influenced by ichthyol-vaseline and other mild forms of treatment.

8. *Wax* may be complicated by traumatization of the canal and drum when removal of wax is attempted. This can be avoided by removing the wax by washing only. Any wound, even the most insignificant, should be given the most careful attention. After a wax plug has been in the ear for a long period of time and is removed, the ear may be so sensitive to noises as to be painful and attacks of vertigo may result. This may be avoided by plugging up the ear for several hours after removal of the wax.

Wax plugs may prove to be inspissated cholesteatomatous masses, in which case there is a chronic *otitis media suppurativa* and necrosis present. These masses are usually very difficult to remove and often after this is done considerable destruction of the tympanic membrane will be present.

9. *Other foreign bodies* of the external ear may act as do wax plugs and cause the same complications. Treatment of these should be the same as for the wax.

10. *Epithelioma*, a minor condition, may progress in its growth to the parotid gland, developing into a serious carcinomatous growth. *X*-ray and radium are curative agents in the uncomplicated epitheliomas; but I have observed the complication of necrosis of the bone of the canal and marked burns following the use of these agents, which required operation. This was no doubt due to the improper or incorrect use of these remedial agents. Palliative *x*-ray and radium treatment is only of value in the complicated or inoperable carcinomas of the external ear, especially where a metastasis into the neck or parotid gland is present.

Complications of Middle-ear Diseases. The first complication one thinks of is mastoid infection; but, as in the consideration of complications of the nose the accessory sinuses are considered a part of it, so are the mastoid cells considered a part of the middle-ear. Consequently, we shall speak of the complications of *tympanomastoid disease* in this connection.

1. *Labyrinth Involvement*. This is the most frequent complication secondary to inflammation of the tympanomastoid. At first there is an irritation or congestion, bringing symptoms of tinnitus aurium, dizziness and vertigo, and later destruction or loss of

hearing and loss of function in the vestibular apparatus. Not only may the nervous mechanism be affected but the bony labyrinth may also become involved in inflammation or necrosis.

2. *The Involvement of the Facial Nerve.* Facial paralysis is a complication especially found where only a thin part of the bone exists between the infected middle ear or the facial canal of the mastoid, or where a real dehiscence is present. The development of a severe congestion through the bone is the explanation of the *modus operandi.* However, a very active process may cause necrosis of the bony canal and thus produce a more severe and often a permanent facial paralysis.

There is a form of facial paralysis in which there is no or very slight tympanomastoid disturbance. In older textbooks this was spoken of as Bell's palsy; but it is now designated as a toxic neuritis. often associated with other nerve or ganglionic disturbances such as tic douloureux, cochlear and vestibular disturbances and herpes zoster. If one makes a very close examination it will be found that the middle ear is seldom absolutely normal in every way. But by far the greatest number of facial nerve complications of middle-ear infections follow operative procedures on the mastoid, expecially the radical operation. The cause is usually due to technical error; however, this complication may result from collateral edema or pressure. When due to trauma and only slight, complete recovery may occur; but when the nerve is subjected to a greater degree of trauma or is completely severed a permanent paralysis results. In such cases only an operation of neuroplasty will be of any value, and I have had considerable experience in hitching the peripheral part of the facial nerve (from the stylomastoid foramen on) to the spinal accessory or hypoglossal nerve. For the mild or lesser injuries of the facial nerve, as well as other forms of facial palsy, expectant treatment is indicated—a mild current of galvanism, faradism or massage of the paralyzed parts may aid. However, lapse of time does more good than anything else, inasmuch as regeneration of the dead nerve must occur, that is, new fibers from the proximal end must grow into the dead peripheral portion. Statement as to an exact time to operate is not well taken. It is much better to depend upon the reaction of degeneration test of the galvanic current than to wait too long, until the nerve as well as the muscles have become atrophied, for in the latter condition a surgically successful union may not result in a regeneration of the nerve.

3. *The Gradenigo Syndrome.* This may complicate a tympanomastoid disease and confuse intracranial complications or meningitis and brain abscess. The syndrome is represented by very severe pain on the side of the face, known as tic douloureux, with an abducens paralysis and labyrinthian symptoms, either cochlear, vestibular or both. These symptoms are produced by the inflammation or infection of the cells in the apex of the petrous portion of the temporal bone and the contiguous dura. The inflammatory process thus presses on the greater trunks of the fifth nerve or even the Gasserian ganglion, the sixth nerve (which is in close proximity) by virtue of its greater length intracranially and the internal ear which is practically located in that part of the temporal bone affected. Recently Dr. W. H. Sears, of Huntingdon, Pa., presented a thesis before the American Triological Society on this subject which, from the standpoint of completeness, is the best I have seen.

The treatment of this complication is conservative or expectant, unless other symptoms point to intracranial involvement, such as a brain abscess or meningitis. In that event a more radical procedure is performed.

4. *Extradural Abscess:* (*a*) *Tegmental, and* (*b*) *Cerebellar or Perisinusoidal*). This complication is fairly frequent and may only be discovered in a well-carried-out mastoid operation, but not before diagnosed. Headache localized over the abscess, associated with tenderness on percussion, may be the only symptom present. At dressings subsequent to a mastoid operation there is often noted a discharge of pus through an insufficient opening. This requires a secondary operation. In the event that this is not done, it is quite likely that a true brain abscess will follow, although it may take some time before real local or focal signs present themselves. The longer it takes for a true brain abscess to develop, the better are the chances for a lining membrane or walling-off process to form.

The brain abscess may develop secondarily by way of the internal auditory meatus, either through the labyrinth or facial nerve. In such cases there need not have been a preëxisting extradural abscess. Another avenue of infection of the brain and formation of a brain abscess is through the medium of the saccus endolymphaticus, which is located on the surface of the petrous portion of the temporal bone. A brain abscess may also develop along the bloodvessel route or from localized meningitis.

The one symptom that should make us think of the presence of an abscess is the constant pain in the head, *headache*, which is not relieved by anything but operation and drainage of the abscess. The *vomiting*, usually projectile or propulsive; the increased intracranial pressure with associated eye-fundus findings, which are dependent upon the size of the abscess; the slow pulse and respirations; the focal signs of a temporosphenoidal or cerebellar localization—are all aids in the diagnosis, but none are pathognomonic.

5. *Lateral Sinus Thrombosis.* When this condition occurs it is ushered in with a chill. The process may be so small as to involve only a small portion of the sinus wall and not necessarily its entirety (circumference). The tendency, however, is to rapidly affect the endothelial lining, causing an accumulation of fibrin and the formation of a clot completely occluding the vessel (Crowe, Beck, Tobey Work).

As this material is washed into the blood stream, the patient has repeated chills with high temperature and sweats. The blood examination invariably shows marked increase in the leukocyte count and a great preponderance of the polymorphonuclears (unless the patient is losing ground). Blood cultures frequently show the causal organisms.

A diagnosis of sinus thrombosis is a clear indication to operate and expose the sinus, turning out the thrombus, obtaining a blood-flow from both sides of the sinus, which is blocked torcularward, and ligating the internal jugular vein. It is best to do the ligation as soon as the sinus is exposed and a thrombus demonstrated, because in the delivery of it a particle may be dislodged and carried down into the vein and into the circulation, causing a secondary complication, such as an infarction.

The exposed sinus, when diseased (thrombosed), is found discolored and harder to the touch. But there are exceptions: I have seen normal-looking sinuses which, when opened, disclosed at least a partial or walled-off thrombosis. A sinus may also be found to contain a liquid thrombus, with absence of the usual resistant feeling.

Puncturing with a hypodermic needle is considered by some (including myself) a questionable procedure in diagnosis, for two reasons: First, the needle may go directly through a partial thrombus and reveal liquid blood, and, second, an infection may be carried into a normal nonthrombosed sinus. This latter condition is unimportant.

A lateral sinus thrombosis becomes further complicated by involvement of the jugular bulb and internal jugular vein, regions which are quite accessible by surgery. However, when the process extends to the superior and inferior petrosal sinuses, and eventually to the cavernous sinus, the operative procedures are more difficult and result in a graver prognosis. Until very recently cavernous-sinus thrombosis was considered a fatal disease, because with the exception of one authentically reported case by Ballance, in which the patient recovered following operation, all patients succumbed. About two years ago Eagleton made his report of his first cure of cavernous-sinus thrombosis following operation. He believed the cure to be effected by ligation of the internal carotid artery, which procedure allowed the sinus thrombosis to become arrested by the stoppage of the adjacent pulsation. Since that time he has added more cases with equally good results. Treatment other than operation is of no value. However, the additional care and medication toward proper elimination of the toxic substances, etc., the support of the patient's vitality by diet, medicine, blood and antitoxins are of distinct value and must be carried out with good judgment and precision. Blood transfusion has saved many a patient just at the turning point. Medications such as intravenous injections of mercurochrome are very much lauded at present. In my own personal experience antitoxins and serums have been of little avail.

*Meningitis.* In every case of extra- or intradural abscess and sinus thrombosis a local meningitis of varying degree is associated. Very often an increase in the cerebrospinal fluid is present, although this may be but very little changed from the normal, cytologically or chemically. This latter form is spoken of as *serous* or *protective meningitis.* Where the infection becomes more extensive, but localized to the dura and arachnoid, it is known as *pachymeningitis;* when the pia mater becomes infected it is a *leptomeningitis* or *generalized meningitis.*

The symptoms of meningitis vary very much, according to the degree of involvement and the type of organism responsible for the infection. A localized meningitis may cause nothing more than a headache, this usually being due to the increased intracranial pressure. However, as the meninges of the brain are continuous with the membranes of the spinal cord, one will soon observe signs referable to the spinal nerves, such as nuchal pain and stiff neck. The general irritability of the patient, a befuddled mind, septic appearance, marked supression of all secretions, small pupils and

often a distinct photophobia are early symptoms of spreading septic meningitis. Reflex phenomena such as Kernig, Babinski, Brudzinski, Shattuck, Oppenheim and Gordon signs are all positive (they may indicate which side is most affected, being more pronounced on one side than the other). An early and important sign of meningitis is the change in the spinal fluid, which is not only increased in pressure but also in cytological, bacteriological and chemical content. The degree of cloudiness is principally an indication of the percentage of pus cells present. Bacterial findings are most important, particularly in determining the type of meningitis present, when differentiating a septic meningitis secondary to a nose or ear condition, or an epidemic meningitis in which there coexists an otitis media suppurative or a suppurating accessory nasal sinus—Streptococcus *versus* Meningococcus Intracellularis.

Cytologically the percentage number of small cells in the fluid denotes the degree of reaction, ten cells to the field being considered a normal content. Chemically there has been much discussion as to the reduction of the alkalization of the cerebrospinal fluid in septic meningitis. The sugar reduction or the copper tests are of value in that they show an infective agent to be present.

The later symptoms of meningitis, such as marked Kernig, dilated or irregular pupils, muttering delirium, involuntary urination and defecation and *taché cerebrale* are of no practical value, since such patients do not recover, the process being no longer limited to the meninges, but the brain itself involved. This secondary complication is a *septic cerebritis* (encephalitis) from which there is no recovery even if the patient survives.

The treatment of meningitis secondary to nasal or sinus conditions has already been described and in no way differs from treatment of meningitis secondary to ear diseases, except there should be in this location a tendency toward abscess formation. The most important thing to bear in mind is that the earlier the original focus—for example, the middle ear, mastoid or labyrinth—is attacked and thoroughly drained externally the better are the chances for recovery. Another fact to be borne in mind is that a localized meningitis always accompanies a brain abscess and lateral sinus thrombosis, so that the sooner and more thoroughly these conditions are cleared up the less chance there is for a generalized meningitis to develop. Finally, a thorough knowledge of the technic of handling brain tissues in these operations is imperative, since too much interference, or too little, will decide the fate of the patient. Repeated spinal

punctures have been practised therapeutically, relieving the pressure as well as the infected cerebrospinal fluid (normal fluid being replaced). The use of the cisterna magna puncture is preferred, since that is much nearer to the seat of the infection. Medicaments introduced into the spinal canal or the cisterna magna, such as urotropin, salvarsan, mercurochrome and serums, have not proven themselves of any value in my practice. However, I am optimistic in this particular therapeutic measure, and prophesy that a substance will be found that will act as a penetrating antiseptic without causing any harm to the delicate intraspinal and intracranial structures. When that time comes the prognosis of this complication will not be so grave.

*Internal Medication versus Surgery.* Operations for a generalized meningitis have thus far been very disappointing, and of 8 cases of operation by drainage of the cisterna magna, performed several years ago, I had only one recovery. This exception was probably of a serous or protective form, although the cerebrospinal fluid had evidence of marked reaction and contained the pneumococci in sufficient quantity to be spoken of as a septic meningitis. The difficulty is that the great pockets at the base of the skull and the sulci over the convex surface of the brain are not drained well, or possibly not at all. However, it is not the fluid that is destructive, but the exudate that is always found in this type of case.

The after-treatment of all these intracranial complications is very important. Symptoms of blockage or progress of the disease must be recognized very early, so as to prevent greater destruction or the formation of new complications, as, for instance, *cerebral* or *cerebellar hernia*, which is spite of all care may result. There are some authors (King) who actually believe that the way to cure a brain abscess is to produce a hernia; but I cannot agree with them, particularly if the hernia be in the location of a vital localizing center (left temperosphenoidal or cerebellar), because of the loss of function of speech or the production of persistent disturbance of equilibrium. Compression of the hernia without obstructing the drainage of the abscess is the best treatment in my limited experience.

*Complications of Nonsuppurative Middle-ear Diseases.* These are the *nerve affections*, either irritative or destructive. From the cochlear region it is the *tinnitus aurium*. The greatest number of middle-ear diseases have this associated symptom, and while it is very annoying it is not serious except on rare occasions. I have seen only one case of suicide actually due to the harrassing noises

in the ear or head. I have, however, seen, as has everyone else, patients who become much depressed or excited from these noises. From the vestibular region one sees cases of dizziness and vertigo, but these are rare as compared with cases of noise in the ear or head. Both noises and dizziness and vertigo are frequently present in a disease that first produces symptoms in the middle ear, namely *otosclerosis*. This most frequently occurs early in the disease when the pathological process is one of spongification.

*Toxic labyrinthitis*, due to some focus of infection such as the teeth, tonsils, sinuses, etc., or lues, is also associated with symptoms of tinnitus and vertigo.

During or after an acute infectious disease, as, for instance, scarlet fever, diphtheria, etc., a marked irritation or destruction of the eighth nerve may result.

A *fracture at the base of the skull* in which the petrous portion is involved, may produce the complication of irritation or destruction of the eighth nerve. Aside from that, these cases carry with them the great danger of the development of a septic meningitis.

A *new growth* developing retrolabyrinthinely on the acoustic nerve produces marked eighth nerve symptoms. But the seventh nerve also is usually involved, especially if the growth is within the internal auditory meatus. As the growth progresses toward the brain, it usually occupies an angle spoken of as the pontine-cerebellar angle, with a very definite symptomatology. The otological examination assists the brain surgeon in the diagnosis by the various functional tests. The radiological examination reveals the internal auditory meatus enlarged, but radio-opaque. The treatment of this complication of the retrolabyrinthine part of the auditory nerve is in reality not within the field of the otologist, unless it be considered on the borderline.

*Luetic labyrinthitis* (osseous) is occasionally complicated either by a gummatous process or necrosis extending from a chronic suppuration of a luetic character. The tympanic membrane in this latter condition will show multiple perforations with smooth borders in contradistinction to a tuberculous process in which the borders or margins of the perforations have a granulation edge. Sequestration is not at all common in the gummatous process and the function of the labyrinth is usually lost. The Wassermann test should be 4 +, but a negative Wassermann with positive symptoms would not alter the clinical diagnosis.

# PROCEEDINGS

OF THE

# SECTION ON GENERAL MEDICINE

JANUARY 26

## Some Problems of the Laboratory as Illustrated by Blood Counts

BY STANLEY P. REIMANN, M.D.

My thoughts are apologetic at presenting this subject in this manner; but, inasmuch as there has been considerable discussion the last number of years and possibly many years before that, if not in antiquity, relative to the science and practice of the professions, particularly medicine, it will probably do no harm to add one more paper. Necessarily, the discussion can cover b ıt a few points. With your permission I will cite cases to illustrate some of the thoughts to be expressed.

A ten-yea -old child brought into the Mary Drexel Home gave the history of having had severe abdominal pain, starting ten or twelve hours previous to admission. It had been generalized and colicky in nature for an hour or two and then had localized definitely in the right iliac fossa. There was moderate tenderness in this region and none elsewhere. Peristalsis was not diminished. The respirations were somewhat increased, but examination of the chest was negative. The temperature was 103° F., and the leukocyte count was 32,000, with 90 per cent polymorphonuclears. Without the leukocyte count this seemed to be a clear case of acute appendicitis. We counselled delay on the score of the leukocyte count, but perhaps also because the child as a whole, to inspection, looked sick. The next morning definite consolidation was found in the base of the right lung. The child ran a typical course of pneumonia and recovered, the abdominal symptoms having disappeared at the time the pneumonia made itself manifest.

There are probably other things in this case to be considered, but the leukocyte count was one of the most, if not the most, important single finding. It may be contrasted with the following:

A man complained of being sick for over a week with symptoms starting as pain in the abdomen, never clearly localized to any one position, but perhaps more so on the right. He had more or less general tenderness over the abdomen, and perhaps more in the right, with distinct rigidity on the right side below the umbilicus. This patient had a temperature of 99.2° F. He had peristalsis everywhere except in the right iliac fossa and there was a vague sensation of a mass in that region. His leukocyte count was 7000, with 70 per cent polymorphonuclears. Four physicians who saw him were of the opinion that he had anything but his real condition.

Dr. Deaver, whose intuitive diagnostic skill is familiar to all, merely said, "We will forget the leukocyte count," a point on which the other physicians had insisted when the possibility of an appendiceal abscess was considered. At operation it was discovered that he had a large abscess, originating in the appendix, with a collection of pus which had been most thoroughly walled off. The patient recovered.

We must remember that the leukocyte count rises, not when the infection is thoroughly localized, but when there is a general constitutional reaction. In this case the leukocyte count was worse than useless, since it was misleading.

We may put it, as a generality, that in order to interpret laboratory findings correctly, it is necessary to have a good understanding of clinical medicine with its background of physiology, pathology, bacteriology and serology, with chemistry thrown in for good measure. A pathologist working with clinicians, therefore, must of course be especially skillful in his own particular field, but he must also be ordinarily skillful as contrasted to especially skillful in the application of his findings to the particular individual under question. This is to say, he must be conversant with clinical medicine to an extent sufficient to appreciate the logic and arguments of the clinicians themselves.

This carries the thought further to the effect that the clinician must be conversant with the logic and arguments of the pathologist. The emphasis, of course, must be laid on the special cases such as we have cited; but, extending this thought, it means to every case, since we must treat patients as individuals and not in masses. The skilled clinician uses his powers of examination, inherent and trained in his five senses; but there is objection to the

clinician who occasionally does laboratory work and then usually in the exceptional case, with the assumption that he is as skilled in this as in his own field. Conversely, there is objection to the pathologist invading the clinical field with similar assumptions. To illustrate some of these difficulties, permit me to cite two more cases:

A woman, aged about fifty years, was brought into the hospital with a history of having had generalized enlargement of the lymph nodes some months before. The diagnosis was never established with any degree of positiveness. She was treated intensively with *x*-ray, whereupon the large lymph nodes became smaller, and at the time of admission to our institution they were just about palpably enlarged. Her spleen, however, was considerably larger than normal. Her blood count showed a mild secondary anemia and 7500 white blood cells. The differential count disclosed immediately that about 10 per cent of the cells could not be placed in the so-called "normal" category and yet they differed from bone-marrow cells or any other cells we were accustomed to see in various well-defined diseases. Counted as large lymphocytes, there was a total of lymphocytic cells to 50 per cent. This 10 per cent of cells showed cytoplasm which was sometimes more granular, sometimes more dense, ofttimes more shadowy than the cytoplasm of normal large lymphocytes. The nuclei also showed pictures which were difficult to interpret. The oxidase reaction gave unsatisfactory results. The *x*-ray treatment was then remembered, and it was thought that she had a lymphatic leukemia with reduction in the number of cells and change in their morphology by reason of the *x*-ray treatment. Arguments *pro* and *con* between pathologist and clinician arrived at no result, until finally a lymph node was removed. This, on section, showed nothing but lymphocytes in the typical picture of the lymph node in lymphatic leukemia.

The clinical pathologist, whether he be working with blood or other substances, requires a particular and peculiar experience which is not to be had by other than specialized work. Furthermore, if the clinical aspects in a broad way are not known and appreciated by the pathologist, he is not only handicapped but at times completely powerless to aid. Incidently this experience reiterates that *x*-ray treatment has opened a new pathology, and the pathologist of today must be a normal histologist, what might be called a "normal pathologist" and an "*x*-rayed-tissue pathologist," all of which add to the sum total of experience he must acquire.

A man died of general peritonitis following ruptured duodenal ulcer. He was brought in *in extremis*, and the blood count showed 15,000 white

cells with a high percentage of polymorphonuclears. At autopsy there were discovered in his liver, spleen and several other organs small collections of cells which looked like myelocytes. Further study proved them to be such. He also had some very moderate general glandular enlargement, with a spleen about three times the normal size. Inasmuch as he had an acute infection, we presume that his blood count increasing to 15,000 was due in large measure to this, and that before the rupture of his duodenal ulcer his blood count per actual number of cells was possibly normal.

Imagine the diagnostic difficulties. This man unquestionably had an aleukemic leukemia. Perhaps he would have shown a few abnormal cells in his blood had it been examined before.

A patient admitted with a diagnosis of primary pernicious anemia, which she had had for a period of a year and a half. The diagnosis seems to have been well established. She was especially interesting because the lymph nodes in the neck, the axillæ, and in the groin had begun to swell several weeks before and on admission were quite distinctly enlarged. Her red blood cells were diminished in number and the hemoglobin likewise, but not quite proportionately. There were nucleated red blood cells discovered in smears. The leukocyte count on very careful examination was normal.

None of the guesses relative to the enlarged lymph nodes proved correct, because on excision of one it was found that there were foci in it with considerable numbers of normoblasts. The pathologist knows that under normal circumstances in the fetus the lymphoid organs as well as the liver show hemopoietic foci. They disappear at or shortly after birth, but reappear in certain cases when demands are made. A rare case surely, but one which expresses very well the necessity for the knowledge and correlation of clinical, pathological and physiological facts to which we might add bacteriological, serological and chemical as well.

This brings up a point of general interest to which attention might be called and that is the unquestioning acceptance by many clinicians of the laboratory tests for various diseases or conditions which are published in such vast numbers in the literature. The process is about as follows: Someone discovers or devises a new procedure for some purpose or other. The results of the tests in a number of patients are published probably with favorable comments. The inventor or discoverer may be a clinician or pathologist or some other specialist. Immediately, the new procedure is accepted by many as an approved undertaking, is tried in suitable or possibly unsuitable cases, and fails to give the desired or accepted results.

On the one hand, the original test may have been published by someone who knew quite well its experimental status, and published the results for what they were worth; others, instead of recognizing this experimental status, accept it as an established fact and expect to obtain information or results in diagnosis and therapy. Disappointment is inevitable because the true relation of affairs is not recognized. On the other hand, the discoverer may have been a closely confined specialist and his knowledge, even though only a working knowledge of more than his own branch, would have been enough to condemn the test before it was born or to place it in its proper relation. This knowledge, especially of the fundamental sciences, is not brought to bear often enough or critically enough upon these new procedures. As a matter of fact, the limitations of the clinical pathologist are recognized clearly by most pathologists themselves but by a less number of clinicians.

Clinical pathologists will admit that their tests are but bits of information and not pathognomonic with few exceptions. If we find the organism of malaria in the red blood cells, the patient has malaria, but there are few clinicopathological findings as definite as this. A story will perhaps illustrate this point. In an army camp I was approached by a medical officer in charge of one of the medical wards. He was carrying a small bottle of saliva, purporting to be sputum. His request was as follows: "Examine this sputum and tell me if the patient has pneumonia," To which I replied, "I cannot tell you from an examination of the sputum (saliva) whether the patient has pneumonia or not." His answer was, "Huh! What good are you?" I told him that I would be glad to percuss or auscultate the patient's chest in an effort to discover whether there was any consolidation present. The reply to this was that such proceedings were none of my business and I had no right to trespass off my domain. This would be laugh-provoking were it not so serious.

Akin to this failure to recognize the limitations is the tendency to place more responsibility upon the laboratory than it has any right to shoulder. From clinicians, this is because: (1) Of the factor just discussed, *i.e.*, failure to recognize limitations, and thus correctly use the laboratory, and (2) to sheer laziness—let the laboratory do it. I have heard it said and have actually witnessed a procedure such as the following: An injured patient is admitted to house or dispensary; the surgeon after a mere inspection of the

injured part says, "Send him up to the *x*-ray." The radiographer sends a report, "Colles fracture, good position," whereupon the surgeon instructs the nurse to apply a Bond splint. Some time later the result is evidently not satisfactory, upon which the *x*-ray and the radiographer are promptly and thoroughly condemned. Was it their fault? The same phenomenon occurs in laboratory examinations. "Send it to the laboratory" is the substitute for work. The discussion which some of us may remember at the meeting of the County Medical Society last year on "A Comparison of the Art and Science of Medicine," irrespective of the many irrelevancies which crop up in such disputations, simply boils down to this: "Do not be lazy, if you are a clinician; do your part, if you are a pathologist: then both of you correlate your results."

Summary. A number of blood counts have been discussed as a text for the general subject of the problems of the laboratory. Any other text might have been used just as well. The evidence points to the fact that a specialized knowledge of the laboratory is necessary for the laboratory man plus an appreciation of clinical ideas. Conversely, the clinician must be similarly equipped in his speciality, with an appreciation of laboratory ideas. It follows that a close coöperation between clinician and laboratory man will obtain the best results from our present knowledge.

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## The Mutual Relations Existing between the Clinic and the Laboratory

BY BOWMAN CORNING CROWELL, M.D.

The subject on which I have been asked to speak to you this evening is the mutual relations that should exist between the pathologist and the practitioner of medicine. If my remarks are made from the standpoint of the laboratory man, it is because I am best qualified to speak from this view-point. I trust, however, that I may be able to emphasize certain phases of the subject that will appeal to the mind of the practitioner, and perhaps aid the worker in deriving the maximum amount of benefit from the laboratory. My remarks will have especial reference to the hospital laboratory, and I may add that, in my opinion, it is essential that relations simi-

lar to those that I shall indicate should exist between the practitioner and the so-called private or commercial laboratory if the latter is to perform its function properly.

In the first place, the man in charge of the work in the hospital laboratory today is a development of recent times. He is required to solve problems of many kinds, morphological, chemical, and humoral, and he must have at his command an insight into the many branches of the medical sciences. His primary requisite, however, is a thorough knowledge of the technical methods that may be applied for the detection of diseased conditions. In so far as he is purely a laboratory worker he deals not with the patient, but with the individual elements that go to make up the patient. To him come the blood, urine, feces, gastric contents, spinal fluid, exudates, transudates, or tissues from the patient, but not the patient himself. In order best to perform his proper function he should be able to make the requisite examinations and to indicate the influence, on the patient, of the abnormal conditions that he encounters in his study of the material submitted for examination. There is no need for him to see the patient or to have a knowledge of practical medicine in order to determine that a Wassermann reaction is positive, that the red cells are diminished in number, or that the amount of creatinin in the blood is increased, but he should be able to point out the causes that may be responsible for these conditions, and the bearing that their presence may have on the patient.

But the final word in the diagnosis, treatment, and prognosis of the diseased condition, or conditions, from which the patient suffers rests with the practitioner. It is his function to apply the information furnished by the laboratory to his own interpretation of the condition of the patient, and for this he should not depend upon the laboratory worker. The latter may give him a detailed report of the laboratory findings of the blood, the urine, the spinal fluid or the tissues of the patient, and their variations from the normal, but the formulation of the diagnosis must rest with the clinician. This presupposes a knowledge on the part of the practitioner of the method of interpreting the results of technical procedures.

The purpose of the clinical laboratory is avowedly and properly to aid the physician in his study of the patient, and both physician and laboratory worker should utilize all available means for the advantage of the patient.

Let me indicate the relations that, in my opinion, should exist between the two workers, as well as deprecate some of the present conditions that exist. Their slogan should be *coöperation*. Inasmuch as the aim of both is, or should be, similar, namely, the advantage of the patient, one should help the other to the extent of his ability, and each should act with due consideration for the work of the other, just as two oarsmen should pull their strokes in unison. The problem, therefore, resolves itself into the best method for securing this coöperation. Let me consider, under separate headings, the various factors that go to make up coöperation, it being borne in mind that I speak impartially and not in a spirit of criticism.

1. *When sending material to the laboratory for examination it is well to specify exactly what mode of examination is desired.* The physician's attention is frequently so fully absorbed during the examination of the patient that this simple rule is neglected, and thus much time and labor are lost to the laboratory man. For example: If pus is to be examined for tubercle bacilli, the nature and importance of the examination should be indicated. At times a microscopic examination of a smear for tubercle bacilli is all that is desired, whereas at other times the examination may be of sufficient importance to justify animal inoculation. If, however, this is not indicated at the time the request for examination is made, valuable material that cannot be duplicated may be lost, and the laboratory be censured unjustly. Simply to make a request for a bacteriological examination of a product generally involves unnecessarily a large amount of work. Similarly, the request for "blood examination," so frequently made, is reprehensibly inexact. Under this same heading a word may also be said in regard to leaving laboratory matters to the discretion of internes. I have frequently known a physician, having a leukocyte count in mind, to direct the interne to have a blood examination made, without specifying the type of examination required. Not being quite certain as to what is in the mind of his chief, and desiring to have the information available when called for, the interne has directed that all the blood examinations of which he could remember the names at the time be made. True, his chief may thus have been satisfied, but at what unnecessary cost to the laboratory man!

2. *Avoid Unnecessary Requests.* Examination of the patient should usually take precedence over laboratory investigations. A

careful examination of the patient will generally yield information as to what laboratory procedures will best aid in clearing up the case, and in the most of the cases only these procedures should be asked for. "Has all laboratory work on the case been done?" This is a question that I have heard repeatedly as the chief was beginning his phyical examination. I refer in this place to unnecessary requests because of their inevitable influence on the morale of the laboratory staff. If a laboratory worker has a consciousness that there is a good reason for making every test, his results will, *ipso facto*, be more reliable and more nearly exact.

3. *The Laboratory Sciences have their Limitations.* This fact should be recognized, and the laboratory should not be held responsible for conditions over which it has no control, or be censured for its inability to do that which is beyond the present scope of the science. This applies perhaps especially to the microscopic examination of tissues. Tissues for examination should be selected carefully, and sufficient information concerning them should be supplied in order to obtain the best results. Frequently if the physician or surgeon is unable personally to visit the laboratory and discuss the case, a brief note on the reverse side of the slip that accompanies the specimen will add a great deal to the information at hand; thus, "This is an interesting case in which there is a question as to diagnosis between a malignant tumor, syphilis, and tuberculosis. The piece is small, it is true, but it is all we could, or will be able to, get." Such a note may lead to animal inoculation for the detection of tubercle bacilli, dark-field examination for treponemata, special fixation for later silver impregnation, in addition to routine morphological examination. All these would have been impossible if the laboratory man had not thus been forewarned. The absence of such a note has often precluded the possibility of formulating an accurate diagnosis.

4. *The Interpretation of Results Obtained in the Laboratory belongs to the Province of the Physician.* This is true as regards the average case, but, from the nature of his work, in individual or unusual cases the laboratory man is often more skilful in interpreting his results than is the physician, and I have never known a case in which the laboratory worker was not willing to place his knowledge at the disposal of the physician.

5. *Any Information that the Physician Possesses that will Aid the Laboratory Man in Making his Investigations of a Case should be*

*Placed at the Latter's Disposal.* I have known many cases in which such information has intentionally been withheld, at times with the intent of not influencing the laboratory man in making his decision, and at other times because it has been said that, in order to incur favor, the laboratory man would make his diagnosis concur with that of the physician. Of course, such a practice can be regarded only as dishonest. If such a laboratory man exists, he should quickly and forcibly be relieved of his duty. So long as a man is being depended upon to do laboratory work he should be entrusted with all the information that may aid him in his work.

6. *Personal Coöperation and Consultation between Physician and Laboratory Worker are Valuable Desiderata.* Personal visits to the laboratory and invitations to the laboratory man to visit the ward and discuss interesting cases cannot fail to be productive of good results to the physician, the laboratory man, and the patient. Real coöperation and an understanding of each other's problems, but not necessarily of one's methods of solution of them, are highly essential. The most successful diagnosticians with whom I have been acquainted have been men who have made it a practice to visit the laboratory in person with more or less regularity. Whether or not this practice stands in the relation of cause or effect to their success may be a debatable point, but I believe that there is a double relation into which both factors enter.

Frozen Sections of Tissues. Although this topic interests especially the surgeon in his relation to the laboratory, I feel that my presentation of the subject assigned me would be incomplete if this were not referred to. Every laboratory should be equipped for making examinations of frozen sections of tissue, as the information thus gained cannot be secured in other ways. It is, however, in regard to the advisability and necessity of making frozen sections for diagnostic purposes while an operation is in progress that there is room for a difference of opinion. Personally, it is my belief that facilities for this work should be readily available to every operating room. The cases in which such work should be done as a rapid method of diagnosis for the surgeon is another question. In no phase of laboratory work is coöperation between surgeon and pathologist more essential. In the first place, thorough training in the selection of suitable tissue for examination and in the interpretation of results secured by this method is a prerequisite on the part of the pathologist. The method is employed most frequently to

differentiate between tumors and other disease processes, and between benign and malignant tumors, and it is here that this coöperation is most often essential. In differentiating between tumors and other disease processes it is the early cases that give rise to the greatest difficulty, and it is precisely in these cases that numerous foci must be examined carefully before the presence of tumor can be excluded. It is obvious that so careful a search is impossible in the time allowed by a surgeon during operation. In the differentiation between benign and malignant tumors not infrequently the surgeon is in doubt and the pathologist has likewise some difficulty in arriving at a conclusion, since he is restricted in his examination to the small portion of tissue submitted to him. It is on that alone that he can base his opinion. If he finds evidences of malignancy, his verdict is of value. If, however, he finds no evidences of malignancy in the sections he examines, this does not preclude the possibility of malignancy being present. In addition to these groups of cases there are many others in which the pathologist can be of real assistance to the surgeon, and he should ever be ready to lend his aid. My confidence in the discernment of surgeons is great, and I feel that frequently their knowledge of a case is more valuable than any information that the pathologist can furnish them, and their instincts should not be unduly influenced by a doubt raised by a pathologist from the examination of a single specimen, or, at most, a few sections hurriedly prepared.

Autopsies. The study of pathological anatomy has been one of the principal factors in furthering the medical progress that has been achieved since the time of Morgagni, during the latter half of the eighteenth century. It was Morgagni who first emphasized the importance of comparing the clinical history with the results of autopsy. That autopsies then became frequent is shown by the fact that the classifications of diseased conditions set forth in Rokitansky's *Handbuch der pathologischen Anatomie* in 1846, when he was forty-two years of age, are said to be based on the results of 30,000 autopsies performed by himself. These figures would tend to show that more than eight autopsies were done every day, including Sundays, during a period of ten years, truly a colossal task: Whether or not these figures are exact, it cannot be denied that this investigator showed an inquisitive spirit of an enviable kind, and set an example that might well be emulated today.

At the present time, in America, the autopsy is not as frequently

performed as it should be. For this condition of affairs we as doctors are alone responsible. In Rokitansky's day it was not the layman who demanded the autopsy, but the surgeon himself, who, through his own efforts, obtained the material for autopsies.

Legislation in favor of autopsies may or may not be desirable today, but without specific legislation every physician who attends a dying patient can accomplish more toward securing permission for autopsy than can be achieved in any other way.

The autopsy serves many purposes. Leaving on one side those autopsies that are performed from the medico-legal and sanitary standpoints, let us consider only those that occur in daily practice. More sick and dying are treated in hospitals today than ever before, but the performance of autopsies should not be limited to those dying within the walls of a hospital. Nevertheless it is to this class of patients that the greatest attention in this respect will be paid for some time to come.

It is my purpose to emphasize the advantages that accrue from an autopsy service, and to state some of the methods by which this service may be increased.

Errors in clinical diagnosis occur daily. Cabot's statistics are probably familiar to all, and if not, they are easily available. Seeking the causes of these errors, we find that they may arise from several sources, which may be classified as follows:

1. Limitations of medical science.
2. Limitations of our individual knowledge of that science.
3. Inaccuracy of observation.
4. Omission of proper diagnostic procedures.
5. Lapses in mental alertness.

It is obvious that each of these causes of error can be diminished by postmortem investigations, but I will endeavor to emphasize this point by an illustrative example. During a cholera epidemic a man entered the hospital with a weak, fluttering pulse, slight rise in temperature, marked prostration, intense abdominal pain, painful diarrhea, and blood-stained dejecta. The patient was at once transferred to the cholera hospital, where he promptly died. The autopsy disclosed the presence of an acute verrucous endocarditis; a calculus impacted in the cystic duct, and bleeding hemorrhoids, but no cholera. Regarded from some standpoints, this may have been a justifiable error, but, on the whole, it exemplifies a number of the causes of error. Certainly mental alertness, proper diagnostic

procedures, and accuracy of observation, coupled with a knowledge of the diseases that were present, might at least have thrown doubt on the diagnosis of cholera.

It is a truism to be remembered that elimination of causes of error leads to greater accuracy in diagnosis, but let us consider this side of the question for a moment and see to what results it may lead. How would the destructive lesion of the chromaffin system in Addison's disease have been found without the aid of autopsies? How would the condition now termed by some a "subacute bacterial endocarditis" have become a distinct entity without the close correlation of accuracy of clinical observation, mental alertness, and postmortem investigations? And how would we know that our clinical diagnoses were frequently inaccurate if we did not have a Cabot to compare clinical and anatomical diagnosis?

I trust that I have emphasized sufficiently the advantages to be gained from postmortem examinations. That these examinations may be obtained with increasing frequency has been strongly exemplified in our own Philadelphia General Hospital. The methods by which this desideratum has been accomplished have been published and can be studied by all who are interested in the subject. I merely wish here to emphasize that an autopsy is an opportunity, and that that opportunity is yours if you care to grasp it. The pathologist can sometimes be of service in the procuring of autopsies, but the real opportunity lies within reach of him who treats the dying and who comes into intimate contact with the family. A word from the chief can often accomplish much more than the arguments or threats of internes, and the interest that each interne has in securing autopsies is usually in direct proportion to the interest of his chief.

In conclusion, is it not true that among the elements that contribute to progress in medicine anatomical studies occupy an important place? We are now in the midst of an era of progress. Preventive medicine has made habitable some of the waste places of the earth by attention to epidemiological factors, such as the elimination of breeding places for vectors of disease, and by the more personal, but also more temporary, expedient of mass inoculations with sera and vaccines. The list of acute infectious diseases that can be controlled by appropriate preventive and curative measures is increasing. *X*-rays and radium are adding to the effectiveness of treatment and strengthening the arm of the surgeon. Chemo-

therapy is making possible the successful treatment of diseases which were formerly treated symptomatologically. Organotherapy has attained a place for itself in the list of valuable methods of treatment. Now the question may be raised as to whether or not accuracy of diagnosis is keeping abreast of the general progress. It is true that the laboratory with its newly devised biochemical and serological reactions is aiding in the recognition of some of the more chronic ailments and the *x*-rays are helping to diagnose hidden foci of disease. But I have already intimated that the laboratory is a mere accessory in diagnosis, which can best serve those who know best what to search for. This brings us back to the man who can best interpret symptoms and physical signs, for it is to him primarily that we must look for progress in clinical medicine. It may be profitable for us to inquire of ourselves how much progress we are making along these lines today, and as to whether this progress is commensurate with the progress in other branches. If not, is not the man who habitually correlates his clinical findings and the actual anatomical conditions in a better position to contribute to progress than he who does not? Such correlation is possible through the agency of an efficient autopsy service, and this is an opportunity that each of us can make for himself.

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## The Clinical Use of Blood Chemistry

BY WITHROW MORSE, PH.D.
(By Invitation.)

(*Abstract*)

Although biochemistry is one of the youngest sciences, the appreciation of its value to medicine is old. In 1790, Lavoisier wrote: "Before hazarding a theory (of disease) we propose to multiply our observations, to investigate the phenomena of digestion and to *analyze the blood*." However, the chemical study of the blood was fostered by few chemists, but the "father of biochemistry,' Felix Höppe-Seyler, gave attention to it in the various editions of his *Handbuch der Chemischen Analyse*. The chemical pathology of the blood was not practicable until Folin, at the Harvard Medical School, began to devise biochemical methods, thus making this science typically an American production. Folin's criterion of the

value of a method was that the method must (1) be accurate; (2) be brief and (3) be applicable to minute amounts of material. Besides Folin, other American biochemists (Benedict, of Cornell; van Slyke, of Rockefeller Hospital, Bloor, of Rochester) have built up a series of methods that are being adopted throughout the world.

The question is asked, "Of what do the chemical studies in a hospital laboratory consist?" In order to answer this question, the speaker analyzed the blood-chemistry reports of the laboratory of blood chemistry of Jefferson Hospital and arranged the results statistically. Of the 1113 bloods submitted during a period (excluding isolated tests for single determinations), 626 were within the bounds of normal, while the remainder were equally distributed between nephritics (240) and diabetics (247). It is necessary to found a set of normals for a laboratory. This should be done by statistical methods. From the results of such studies of over 1000 cases the following normals are used in the laboratory mentioned: (Alongside are given the normals accepted in two European countries).

| | Per 100 cc. of blood. | | |
|---|---|---|---|
| | Gm. | German. | Norwegian. |
| Non-protein Nitrogen | 27.0 | 25 to 40.0 | 23.7 to 41.0 |
| Urea Nitrogen | 14.0 | 10 to 18.0 | 10.5 to 22.2 |
| Uric Acid (Dry) | 4.0 | 1 to 3.5 | 2.4 to 4.6 |
| "Creatinin" as such | 1.5 | 1 to 2.0 | 1.0 to 1.3 |
| Plasma Chlorides | 540.0 | 500 to 650 | |
| Sugar | 80.0 to 100 | 60 to 110 | 98.0 to 111 |
| Cholesterol | 150.0 | 150 to 180 | |

The following states have characteristic variations in blood constituents from the normal:

| Disease. | Characteristic variations. |
|---|---|
| Nephritis | Nitrogen Retention. |
| Nephrosis (Nephritis with Edema) | Normal or Low Nitrogen; Hypercholesterolemia. |
| Obstruction (Prostate) | Progressively High Nitrogen. |
| Intestinal Obstruction | High Nitrogen; Low Chlorides. |
| Gout | Normal Nitrogen, Except during Attacks. |
| Bichloride Poisoning | Great Retention of all Constituents. |
| Toxemias of Pregnancy | Low or Normal Nitrogen. |
| Diabetes Mellitus | Hyperglycemia. |
| Renal Diabetes | Blood-sugar Normal One Hour Post-prandial |
| Biliary Calculi | Hypercholesterolemia. |
| Lipemia (Diabetic) | Hypercholesterolemia. |
| Syphilis | Hyperglobulinemia. |
| Acidosis of Childhood | Increased Sodium. |
| Infantile Tetany | Low Calcium. |
| Nephritic Acidosis | Increased Inorganic Phosphate. |
| Rickets | Low Phosphorus. |
| Cyanosis | Increase in Unsaturation up to 6 Volume Per Cent. |

Two curves were shown of the so-called "creatinin" quantities, normal and involved. The curve of normal is an isometric curve with the peak at about 1.5 mg. per cent. The curve for creatinin in cases of retention is a skew curve with the peak at 1.70 mg. per cent and the fall gradual to the highest figure (7.50 mgs. per cent) obtained in this laboratory. The lowest observed creatinin was 1.25 mg. per cent. The value of "creatinin" as a diagnostic agent is evident, even if the chemist (S. R. Benedict) finds that it is improbable that the "creatinin" is true creatinin.

Diagnosis must be made with great care from the blood data reported by the laboratory. Thus, it is frequently said that the ratio N.P.N. : urea nitrogen is 2 to 1 in normal cases and that departure from this ratio is indicative of disease. Twenty-five blood analyses were shown in which the ratio variations of from $-3.2$ to $+10.8$ occurred (that is, $2 \times$ urea $17.2 = 34.4 =$ N.P.N. $23.6 + 10.8$).

In closing, it was urged that the chemist in charge of the blood chemistry should not be held responsible for interpretations of results and should under no circumstances be called upon to diagnose the disease. His responsibilities are great enough as chemist to insure that the reports are accurate. Bloods submitted for chemical analysis should be handled objectively, without any preconception as to the disease concerned or suspected. It is necessary, however, that the chemist be assured that the blood has been collected properly and that dietary and therapeutic measures that may cause modification of the findings be given to the laboratory when the specimen is submitted.

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FEBRUARY, 23

## The History of Appendicitis

BY J. VERNON ELLSON, M.D.
(By Invitation.)

When we mention a "history" our thoughts are apt to refer back to ancient times, to people far remote from our own existence; but the history of appendicitis is a modern history of comparative recent times.

Galen, who of all the ancient writers gave by far the most complete anatomical descriptions, ignored this important organ, and it is thus readily understood that those who immediately followed him and even the medical writers of the Middle Ages made no mention at all of the appendix. The first reference to this structure was found in a work on anatomy published in 1522 A.D. by Berengarius Carpus, professor of surgery at Pavia and Bologna, in which he speaks of there being found at the end of the cecum a certain "additamentum," "empty within and in breadth less than the smallest finger of the hand and of a length of 3 inches or thereabouts." It is probable that this observation was original with him.

Andreas Vesalius further calls attention to this structure in his *Anatomy*, published in 1543, with several illustrations showing the appendix curled upon itself; while Stephanus, at Paris, in 1545, makes no mention of the appendix, but, curiously enough, pictures it on one of his plates.

Later, such men as Ambroise Paré and Fallopius mention it in their writings, while Morgagni, in 1706, devoted considerable space to its description and called attention to the fact that the appendix did not hang down from the cecum, as previously pictured, but emptied itself down into the cecum.

As a disease entity it is probable that Hippocrates first recognized appendicitis with abscess formation when he said: "Suppuration upon a protracted pain of the parts about the bowel is bad." It is interesting that Peter Lane, in 1612, states on the authority of Lonicerius that "Hippocrates did die of this disease," and it was known for centuries under the rather vague name of "iliac or colic passion."

It was not until 1759 that Mestivier reported a fatal case of abscess on the right side of the umbilicus, from which a pint of pus was evacuated by incision, found at the postmortem examination to be due to perforation of the appendix which contained a large rusty pin; he attributed the perforation to the pin. After this many cases were reported where autopsy findings showed foreign bodies in the appendix, as parasitic worms or even lead balls which the patient had been made to swallow (in the hope of overcoming an intestinal obstruction).

There followed a great confusion of ideas as to the probable cause and the best mode of treatment of what was now known under the names, typhlitis, apophysitis, ecphyoditis, epityphlitis, peri-

cecitis and scolecoiditis. In 1812 Parkinson, a London physician, presented a case of fatal peritonitis in which he plainly recognized the perforation of the appendix as the cause of death, and in 1827 Mélier described with considerable accuracy the diseases of the appendix and went so far as to say: "If it were possible to establish with certainty the diagnosis of these affections we could see the possibility of curing the patient by operation. We will, perhaps, some day arrive at this result;" but his article appears to have gained little or no recognition, probably due largely to the fact that Dupuytren, the greatest surgical authority at that time, held the view that these abscesses in the right iliac region developed around the cecum, outside the peritoneum, but were capable of causing inflammation in this membrane. Other writers later insisted on the appendix as the cause of the disease.

Out of this confusion, in 1886, came the article of Reginald Fitz, of Boston, which convinced the medical world of the practical truth of the contention that in all inflammations of the right iliac fossa the vermiform appendix of the cecum was the cause of the trouble. In this article the term "appendicitis" is first used and quickly displaced all other terms with slight opposition. This epoch-making article seemed to simplify and clarify the entire situation. McBurney, in 1889, added another great advance in the diagnosis of appendicitis when he described one definite spot (which now bears his name) as the point of localized pain and tenderness almost invariably found in cases of inflammation of that organ.

In treating this condition, surgical intervention was postponed until the last possible moment when an abscess was actually pointing; but, as early as 50 B.C., we have an instance cited by Aretaeus in which he incised and evacuated pus from what may have been either a large pyonephrosis or appendiceal abscess. In more recent years a great variety of treatments was developed, chief among which were the use of hot applications, blood-letting, swallowing gunshot lead balls, while sedatives were used sparingly and purgatives freely, with incision of the abscess when fluctuation was noted, and it was not until 1848 that Hancock, an English surgeon, performed the first deliberate laparotomy for periappendicular suppuration and proposed such treatment for all cases with abscess before pointing or fluctuation had occurred or even before adhesions to the anterior abdominal wall had formed. Early in the nineteenth century, Graves and Stokes, of Dublin, were advocating the use of

opium in large doses, and Hancock took advantage of this, but did not have the aid of drainage tubes, which Chassaignac introduced in 1859. Willard Parker, of New York, had in 1847 performed early incisions, but not until 1867 was he fully convinced of the advisability of the procedure and urged early incision in all cases with abscess formation; this was then widely adopted, further aided by the introduction of antisepsis, reducing the risk to a minimum.

Although in 1884 Samuel Fenwick had said that "it would seem to be much better if we could cut down directly on the appendix as soon as the diagnosis was tolerably certain, tie it above the seat of perforation and remove from its neighborhood any concretion or decomposing material that might be the cause of irritation," and Prof. Mikulicz, of Krakow, had urged "that every form of perforation of the stomach and intestine should be treated by opening the abdominal cavity and suturing the perforation," it remained for Krönlein, of Zürich, in the same year, to perform the first celiotomy followed by removal of the appendix, for on February 14, 1884, he operated on a boy, aged seventeen years, making a midline incision from the umbilicus to the pubis, washed out the fibroserous exudate found there with 2.5 per cent carbolic acid in warm water and, finding the appendix perforated, deliberately removed it. The boy rallied, but died two days later, and Krönlein states that no autopsy could be secured as the operation was performed in a private house. This is not the first case of the removal of the human appendix during life, for in 1735 Claudius Amyand, F.R.S., had operated on a boy, aged eleven years, for the cure of a discharging sinus in the right thigh associated with an irreducible scrotal hernia, and during the operation found the hernial sac to contain the appendix perforated by the point of a pin. In removing the pin he perforated the appendix still further and then deliberately ligating and removing the appendix, completed the operation.

R. J. Hall, of New York, performed the first operation on the appendix in the United States, in May, 1886, while operating with a probable diagnosis of strangulated hernia, on a boy, aged seventeen years, and finding the vermiform appendix curled upon itself and having near its base a small oval perforation, he ligated the appendix, freed it from its adhesions and removed it; and as he claims, "I have been unable to find any case of perforative peritonitis due to the ulceration of the vermiform appendix successfully treated by laparotomy and resection of the appendix itself," for it will be remembered that Krönlein's case did not recover.

To Thomas G. Morton, of Philadelphia, belongs the credit of the first successful operation for the removal of the appendix deliberately undertaken with the diagnosis of disease in that organ. The operation was performed on April 27, 1887, and reported by Dr. Frank Woodbury the same evening to the Philadelphia County Medical Society, in a brief paper entitled, "Laparotomy for Perityphlitic Abscess," showing at the same time the specimens which "consist of the vermiform appendix, which is perforated by an ulcer, and a piece of omentum infiltrated with lymph." In the report he states that the operation was performed by Dr. Morton, assisted by Drs. Wilson, Rhodes and himself. This case was reported in detail on June 1, 1887, by Dr. Woodbury before the College of Physicians of Philadelphia[1], as follows:

"I have the honor of presenting to the College this evening a private patient who, five weeks ago today, was apparently in articulo mortis with perityphlitic abscess. Laparotomy was skilfully performed by Dr. Thomas G. Morton, the abscess evacuated and the appendix vermiformis removed at its origin, almost divided by an ulcer. I also present the specimen taken from the patient, consisting of the vermiform appendix almost divided by an ulcer; also a portion of the omentum, which was included in the abscess and removed with the appendix. Accompanying these is a small fecal or phosphatic concretion resembling in size and general appearance a small cherrystone (which it was at first supposed to be), which evidently was the cause of the ulceration. The notes of the case are briefly as follows:

"Case Report I.—Perityphlitic abscess; amputation of the vermiform appendix; recovery. Charles M. N. K., aged twenty-six years, born in Philadelphia, paperhanger by occupation, not married, of spare frame and of good habits, had always had good health except that for the last three or four years he had been subject to sudden and severe attacks of abdominal pain. These attacks came on without warning while he was in excellent health and would completely prostrate him. Pain was of a stabbing character and was most intense across lower part of the abdomen and especially around the umbilicus; it was attended by great irritability of both bladder and rectum; sometimes there would be watery diarrhea, but there was always a marked increase in the amount of water voided, the urine being red, "like blood," in color. He is of the opinion that he has at times passed blood in his urine. The attacks, often lasting a few hours, usually passed away gradually, leaving him rather weak for a short time, but he rapidly recovered and enjoyed uninterrupted good health until the next attack came on. I first saw him on April 20, when he came to my office complaining of having taken cold. He looked haggard, skin and con-

[1] Case of Exploratory Laparotomy followed by Appropriate Remedial Operation. Woodbury, Frank, M.D., Professor of Therapeutics, Materia Medica, and Clinical Medicine in the Medico-Chirurgical College of Philadelphia, Trans. of College of Physicians, Third Series, 1887, ix, 18. Read June 1, 1887.

junctivæ rather sallow, tongue coated, no appetite, and bowels constipated. He said that he felt miserable and had pain in his muscles in different parts of his body. He had frequent micturition and was passing a remarkably large amount of pale urine. At this time he did not complain of abdominal pain. He was given fractional doses of calomel and soda bicarbonate with pepsin and directed to keep in his room. The urine examined when he returned next day contained a large proportion of albumin (one-fifth on boiling) and under the microscope showed many leukocytes and a few hyaline casts.

"April 22: Felt nauseated during the night and took mustard water to cause emesis. Bowels had been moved satisfactorily with small doses of calomel. After taking the mustard water he vomited, but was not much relieved. During the day had great irritability of the bladder and was much prostrated. When he came to my office he was so weak that he had to rest an hour and take stimulants before he could go home.

"April 23: Spent the day lying upon a couch, now complaining of abdominal pain. He had not slept and was very restless. Bowels not moved for two days. Repeated calomel in fractional doses ($\frac{1}{10}$ gr. every hour until five doses were taken) and ordered quinine hydrochlorate gr. 12 daily, poultices to abdomen.

"April 24: At morning visit found that during the night he had suffered intensely and did not sleep at all. Bowels not yet moved. Ordered cupful of hot water every hour to assist the action of calomel given yesterday. In the afternoon he had several copious movements, but the pain persisted. He indicated the point of greatest tenderness about midway between the umbilicus and the middle of Poupart's ligament. A resisting mass the size of a small egg could be detected upon deep pressure in this locality, but examination caused severe pain. Morphine sulphate in $\frac{1}{2}$-gr. doses was given every two hours until the pain was relieved. Poultices again applied over abdomen. Temperature 103.5°; pulse 140. On the 25th, had a very bad night, pain in tumor very excruciating, swelling somewhat larger and very tender. Skin not discolored, tumor evidently beneath the peritoneum. Passed urine, which was said to contain small blood-clots. Dr. James Wilson saw the case in consultation. Diagnosis either intussusception or perityphlitic abscess. Ten foreign leeches were applied over the spot of tenderness, with great relief to the patient. Morphine sulphate and quinine were continued.

"April 26: Skin around leech-bites inflamed; tumor more flat and very tender, apparently nearer the surface. Bowels not moved since the 24th. A pint of warm sweet oil was thrown into the colon with a large tube: this felt comforting and later produced evacuation of the bowels.

"April 27: Skin around leech-bites more swollen, injected and tender: the right lower half of the abdomen was dull on percussion, the dulness extending over the midline from a point just above the anterior inferior spine of the ilium; external to this the percussion note was clear. General condition poor; face pale, features pinched, beads of perspiration on forehead. It was decided on consultation with Dr. Wilson that opening the abdomen would be justifiable. Dr. Morton saw him at 11 A.M. At 2 P.M.

laparotomy was performed. The leech-bites were noticed to be separating. An ounce of whisky was given before ether was administered. The field of operation was cleansed with soap and water, and neighboring hair removed; the surface was again washed with ether, followed by corrosive sublimate 1 to 2000. The usual antiseptic precautions were observed as to instruments and field surrounded by towels wet with the mercuric solution. The incision was made directly over the swelling and, finding the muscles infiltrated with pus, it was extended until it measured 10 inches, commencing just above and 2 inches to the right of the umbilicus, it continued obliquely downward to the pubis. The peritoneum was opened and a free flow of pus followed having a decidedly fecal odor. In it was found a concretion resembling a cherrystone, the vermiform appendix was greatly swollen and exhibited a perforated ulcer extending three-fourths around its circumference and very near to the point of origin. A silk ligature was applied close to cecum and at the terminal portion of the appendix, and the intervening portion comprising almost the whole organ was removed, together with a large portion of the omentum which projected into the abscess cavity, the walls of which were then scraped with a curette and douched with simple warm water.

"Following the operation he entered upon convalescence, which was uninterrupted. He was entirely free from abdominal pain, except from distention of the bladder, requiring the use of the catheter for a week. The bowels were moved on May 1, after he had yolks of two eggs and milk. The temperature fell after operation and did not rise again above 100° F. The drainage-tube was removed piecemeal; the last portion was taken away on May 13. He sat up on May 11 and rapidly regained strength. He was out riding May 21. His recovery was assured by careful nursing, the administration of a small quantity of whisky, a teaspoonful every two hours, and the use of Bovine and the Hoff's extract of malt, at first every two hours fluidounces ½ of each, lately has been taking it four times a day. At present the wound is healed and he appears to be in his usual health."

At this same meeting Dr. Morton discussed another case similar to this one, a woman, from whom he had removed a perforated appendix on February 1, 1887, but she died from shock three hours later. But in comparing these apparently analogous cases, one with a successful outcome, the other terminating fatally, Dr. Morton raised the question as to the advisability of removing the human appendix, to which Dr. Chapman replied: "A true vermiform appendix is found in only six animals, viz.: man, gorilla, chimpanzee, orang, gibbon and the wombat. There can be no doubt, therefore, that the cecal appendix is one of those parts of the human body having no particular significance, being of use only in animals where it is expanded so as to supplement the function of the stomach. In the human being it ought to be removed with

no bad effect whatever. . . . So that I thoroughly agree with Dr. Morton in what he has said about opening the abdomen and taking out the appendix. It seems to me that the human being is better off without the appendix than with it, for it is nothing but a trap to catch cherrystones and other foreign bodies!" This case was again discussed before the Philadelphia County Medical Society on December 14, 1887, at a symposium, on "Pericecal Inflammation," when Dr. J. H. Musser spoke on the "Morbid Anatomy," Dr. William Pepper on "Diagnosis," and Dr. Thomas G. Morton on "Treatment," with discussion by such men as Dr. John H. Packard, Dr. William Osler and Dr. W. W. Keen. At this meeting Dr. E. Montgomery raised the question whether it would be better to do laparotomy for the purpose of removing the appendix "when the inflammation subsides," in cases subject to recurrences of pain and tenderness in the right inguinal region. Although this case was given the alternative diagnosis of intussusception or perityphlitic abscess by Dr. Woodbury and Dr. James C. Wilson, there can be little doubt from the subsequent discussions and the literature that Dr. Morton, himself, operated with the view that the appendix was the seat of the trouble and deliberately sought out that organ; and in this he may have been actuated by the fact that he, himself, lost a brother and a son with the same disease.

On December 30, 1887, H. B. Sands, of New York, operated for disease of the appendix and published the case on June 16, 1888, stating that "I diagnosticated the case as one of acute septic peritonitis caused by perforation of the vermiform appendix and advised an immediate resort to laparotomy. I am acquainted with no case like mine in which a perforative peritonitis due to disease of the appendix has been diagnosticated and treated by laparotomy with a favorable result." Of Morton's case he apparently had not heard.

That this operation of Morton's marked one of the most important and radical advances of modern surgery is well evidenced from an article that appeared in the *Medical News*, August 6, 1892, entitled "Timely Operations for Appendicitis," in which the editor states:

"Among those to whom greatest credit is due for what amounts to a revolution in professional opinions are Thomas G. Morton, of Philadelphia, and Charles McBurney, of New York. Other surgeons are also worthy of distinguished mention, but recent papers by the two operators named have reawakened a sense of obligation to them. . . . To Morton must be given the credit for having deliberately sought out and removed an

ulcerated appendix and for having, by his paper before the Philadelphia County Medical Society, first clearly established the principles of surgical treatment of pericecal inflammation. (Dr. Woodbury's case is again presented.) . . .

"Thus Philadelphia may claim the greater share for the credit for what may justly be called one of the most important and most radical advances in modern surgery. 'Morton's operation,' as it deserves to be called, is a different thing from the procedures formerly indulged when the abdomen was simply opened by a 'Willard Parker' incision to drain an evident abscess. . . . Rarely has a discussion before a medical society been productive of more good than that historical discussion before the Philadelphia County Medical Society on December 14, 1887, for from that discussion may justly be dated the modern advance in the treatment of appendicitis."

This article called forth a question of priority by Sir Frederick Treves, in a letter to the *Medical News* on August 6, 1892, in which he calls attention to a case reported by him, stating that, "In 1886 a patient with relapsing case of typhlitis came under my care in the London Hospital and after due consideration I proposed to 'deliberately seek for and remove' his appendix. I operated upon him during a period of apparently good health, on February 16, 1887, and was able to correct the distortion of the appendix without actually excising it. He made a perfect recovery. On September 19, 1887, I brought the matter before the Royal Medical and Chirurgical Society. The paper was read February, 1888," and it is found recorded in the *Lancet* for 1888, under an article entitled, "Relapsing Typhlitis Treated by Operation," which makes no mention of the dates of operation nor the manner of dealing with the appendix.

This does not detract in any way from Morton's work, for any claim to priority in medicine or surgery always rests, by the consent of the profession, not upon date of performance, but upon date of publication. Moreover, Treves' operation, while having the same organ in view, was essentially different, being of an orthopedic and not exsective nature; it is the difference between a plastic operation upon a limb and an amputation; and, as a matter of fact, it is Krönlein who is entitled to credit for first removing the appendix.

The subsequent history of the treatment of diseases of the appendix is one of growing boldness of surgeons the world over, especially in America, in opening the abdomen and removing the diseased organ, evolving at the same time a special technic of the

new operation until it has become well stabilized and is one of the most frequent of surgical procedures and we of Philadelphia can feel a justifiable pride in this work of one of our surgeons.

In presenting this paper we wish to acknowledge our special indebtedness to Dr. William J. Taylor, for his valuable assistance in locating the original articles and for access to the Library of the College of Physicians.

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## Electrocardiographic Studies on a Case of Attempted Suicide with Digitalis

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AND

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(By Invitation.)

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The patient who forms the subject of this report was admitted to the Philadelphia General Hospital on June 17, 1924. He was obviously psychopathic and gave a weird history of being commanded by "Spirits" to end his life by drinking as much digitalis as he could buy for one dollar. This occult order he proceeded to obey on June 16, one day previous to his admission to the hospital. By finding the bottle, we were able to substantiate in a measure his story that he had taken at one dose 2 ounces of tincture of digitalis.

Due to his mental condition, which was diagnosed as paresis, a satisfactory history could not be obtained. There had probably been mild cardiac symptoms over a period of months, for digitalis had been prescribed in the past. Examination revealed nothing

striking. There was definite though not excessive arteriosclerosis. The heart was little if at all enlarged: the left base measured 12 cm., the right base 2 cm. There were no murmurs heard. The lungs were moderately emphysematous. There were no signs of cardiac failure. We thought it important to establish as well as we could the state of the cardiovascular system. To sum up our opinion without going into details, there was definite damage to the vascular system and the heart likewise probably was the seat of a moderate amount of sclerosis. The only physical sign of the latter was moderate cardiac enlargement. There were no definite signs that we could elicit of myocardial insufficiency. He had been able to perform his work as a street-cleaner up to the time of his admission to the hospital. In short, for a man apparently much older than the sixty-four years he admitted to, we concluded that his heart was quite efficient, though slightly damaged. The kidneys were negative. The Wassermann reaction was strongly positive, both in the blood and spinal fluid. The blood-pressure was 108/60.

Neither when first admitted nor at any subsequent time was his condition alarming. However, he was probably in considerable potential danger, and very uncomfortable because of vomiting.

Discussion. *Disturbances of Rhythm.* On admission or twenty-four hours after the ingestion of the drug, electrocardiograms showed a high degree of A–V block. The block was irregular and unstable. At times the conduction was 2 to 1. Other cycles showed 5 to 1 conduction. The block was unstable. The exertion incident to vomiting caused the ventricles to follow the auricles beat for beat, though the P–R interval remained greatly prolonged.

The auricular mechanism at this time is of interest. The auricles were contracting at the rate of 140 per minute in response to impulses apparently of normal sinus origin. A sinus tachycardia as a result of digitalis is a distinctly unusual mechanism. In a series of cases in which the toxic effects of digitalis were studied, Reid[1] encountered this mechanism twice. In a similar series reported by Luten[2] 4 addition instances are recorded, either with or without ventricular dissociation.

On the next day, forty-eight hours after the drugs was ingested, electrocardiograms showed a nodal rhythm with both auricles and ventricles responding at the rate of 90 per minute. After the hypo-

[1] Jour. Am. Med. Assn., 1923, lxxxi, 435, and Arch. Int. Med., 1924, xxxiii, 23.
[2] Arch. Int. Med. 1924, xxxiii, 251; ibid., 1925, xxxv, 74; ibid., 1925, xxxv, 87.

dermic injection of atropine sulphate gr. $\frac{1}{30}$ this gave way to a sinus rhythm with periods of A–V dissociation. On the third day of his stay in the hospital the rhythm was normal. On giving atropine, however, we again set up a nodal rhythm.

To sum up, the disturbances of rhythm noted in this case were: (1) Inverted *T*-waves; (2) a rapid auricular rate or sinus tachycardia; (3) high-grade heart-block; (4) nodal rhythm of a fairly rapid rate; (5) in the early stages of an atropine effect, A–V dissociation with the ventricles beating more rapidly than the auricles; (6) a negative finding: no extrasystolic impulses.

Robinson and Wilson,[1] in studying effects of digitalis in progressively increasing amounts up to the lethal dose on the hearts of cats, found a pretty definite and constant sequence of events to occur. These were: (1) Inversion of the *T*-wave; (2) depression of A–V conduction; (3) after larger amounts increase in the rhythmicity of auricles and ventricles, the ventricular rate soon exceeding the auricular rate and thus causing A–V dissociation; (4) at about this time idioventricular complexes made their appearance, quickly followed by idioventricular rhythm with abnormal ventricular complexes; (5) ventricular fibrillation.

Luten[2] has recently reported a series of 4 cases of digitalis intoxication in which he found essentially this sequence of events to occur in human hearts poisoned with this drug. If this is so, our case had not quite approached the point of dangerous toxicity—that of ventricular ectopic tachycardia and ventricular fibrillation, though it had approached to the stage of rapid auricular and ventricular action and A–V rhythm.

*The Amount of the Drug Active in this Patient.* So far as we can discover, this is the largest single dose of digitalis to which a human heart has been subjected. Actually there are instances on record where hearts have been brought gradually under the influence of larger amounts of digitalis than was this heart.

Eggleston[3] has devised a method whereby the doses of digitalis can be calculated in relation to the weight of the patient. He has found that a definite therapeutic effect can be produced by administering digitalis in the proportion of 1 cc for every 10 pounds of body weight. The full therapeutic dose therefore for our patient who

[1] Jour. Pharmacol. and Exper. Therap., 1918, x, 49.
[2] Loc. cit.
[3] Arch. Int. Med., 1915, xvi, 1.

weighed 130 pounds would have been 13 cc. Actually by taking 2 ounces of the drug he ingested practically 500 per cent of the therapeutic dose. One case in the series of Reid[1] received 700 per cent of the therapeutic dose. This patient developed auricular fibrillation and recovered. Another of his series received 500 per cent of the therapeutic dose. This patient developed ventricular fibrillation and died.

One of the striking facts about our case was the relative mildness of the toxic effects from so large a dose of digitalis. Several factors might account for this. The drug might not have been entirely absorbed, or the particular sample used might not have been active. A third reason is that this particular heart may not have been susceptible to digitalis in so far as the development of ventricular tachycardia and ventricular fibrillation were concerned.

Pardee[2] has shown that the body excretes or destroys from 10 to 40 minims (average 22 minims) of digitalis per day. Granting this and accepting the average figure it would take forty days to rid the body of 2 ounces of digitalis. In the case we are reporting, it took but twenty-four days for the *T*-wave to reach its maximum upright deflection. This discrepancy between the observed twenty-four days and the calculated forty days might in part be accounted for by the fact that the excretion figure of 22 minims is an average figure and that many cases in Pardee's series excreted as much as 40 minims per day. Another factor that might also help to account for the discrepancy is the fact that there can be present in the body a certain amount of digitalis without its causing any definite changes in the electrocardiogram. However, using the average excretion figure of 22 minims per day, we find that there would have been absorbed approximately 9 drams of the drug. If we allow another 2 drams as the amount that might be present in the body and not cause electrocardiographic changes, it seems fair to say that at least $1\frac{1}{2}$ ounces of the 2 ounces ingested were absorbed. It cannot be said however with certainty that the whole of the ingested amount was not absorbed.

We feel that a weak preparation of the drug was not a factor responsible for the relatively mild phenomena exhibited, for the reason that those toxic states that did occur were exceedingly severe. This is particularly so as regards A–V conduction.

[1] Loc. cit.

[2] Jour. Am. Med. Assn., 1919, lxxiii, 1823.

We feel that there is some evidence to show that this particular heart simply was not susceptible to the development of extrasystolic arrhythmias. The implication that certain hearts develop certain arrhythmias under digitalis while other hearts do not is borne out by comparing some of the other instances of digitalis intoxication that have been reported. In one of the cases of Reid's series ventricular ectopic tachycardia and ventricular fibrillation developed after the ingestion of only 148 per cent of the calculated therapeutic dose. In another of his cases high-grade heart-block and A–V dissociation developed after only 83 per cent of the therapeutic dose had been ingested.

SUMMARY. 1. A single case is reported in which 2 ounces of tincture of digitalis were taken at one time in an effort to commit suicide.

2. The normal heart rhythm was markedly disturbed. The arrhythmias recorded were, high-grade heart-block, a rapid sinus tachycardia, nodal rhythm, and seven minutes after the subcutaneous injection of atropine sulphate, grains $\frac{1}{30}$, transient A–V dissociation with a ventricular rate more rapid than the auricular rate.

3. At no time was the patient critically ill. This is accounted for by the fact that probably not all of the ingested drug was absorbed and also by the fact that this particular heart was not prone to develop extrasystolic arrhythmias.

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## THE DIAGNOSIS AND TREATMENT OF PULMONARY TUBERCULOSIS

BY A. H. PERSKY, M.D.

(By Invitation)

THERE are those who believe that the status of the diagnosis and treatment of pulmonary tuberculosis has become more or less fixed; but the tuberculosis problem, as every other field of medicine, is a growing one, and needs from time to time a revision or stock-taking if only to reëmphasize certain well-known facts, to say nothing of what such a revision may show in the way of progress that is being made. I shall say something of diagnosis as deter-

mined by a careful history-taking, and an appreciation of physical signs and laboratory aids. I shall also say something about some present-day conceptions of the treatment of tuberculosis. My remarks on this subject are the result of an experience gained in the clinics of the Henry Phipps Institute, the City Chest Clinic at the St. Agnes Hospital and the ward service of the Rush Hospital.

By far the most important factor in diagnosing a case of tuberculosis is the taking of a careful history. This stands out preëminent. Frequently, in spite of negative physical findings and negative *x*-ray reports, cases are diagnosed "positive" entirely on the strength of the history—that is, a history of hemoptysis, pleurisy, hoarseness, cough, contact, etc.—a positive diagnosis which is later substantiated by the course of the disease.

1. Landis states that the one disease above all others in which hemoptysis most frequently appears is pulmonary tuberculosis. There still seems to be a marked hesitancy among physicians to diagnose such a case as tuberculosis, either tentatively or positively. It is not due usually to carelessness. There are many physicians who would rather make a diagnosis of nontuberculosis, and so jeopardize the patient, than to make a positive diagnosis for the false fear of placing the stigma of the disease on the patient. This is particularly true where there are indefinite physical findings. I cannot impress too strongly this one symptom of hemoptysis. It stands out preëminently. Cabot states that while he does not deny that the causes of hemoptysis are numerous, yet the cause of genuine obscure hemoptysis is only one, namely, pulmonary tuberculosis. In the face of such definite teaching, men will still ascribe to all other diagnoses than the most obvious one.

2. Pleurisy, with or without effusion. Varying with different authorities, the general statement is made that from 80 to 90 per cent of all cases of insidious pleurisies with effusion are due to tuberculosis. Occasionally there may be a history of acute cold; frequently there is no history of exposure. When we have a history of repeated attacks we can almost certainly make a tentative diagnosis of tuberculosis. The importance of this symptom is, also, too frequently disregarded and the patient is treated symptomatically.

3. When we have a history of transient attacks of hoarseness over a period of time we should view this with suspicion. Some authorities have stated that 80 to 90 per cent of these attacks are tuberculous in origin, usually secondary to a pulmonary focus. Therefore,

in the presence of such a history, a most careful examination of the lungs is indicated.

4. With a history of cough and expectoration of longer duration than six weeks every effort should be made to rule out pulmonary tuberculosis. While the symptom may be due to a great diversity of causes, tuberculosis should never be forgotten; the burden of proof rests with us. It is well to remember that coughs which do not yield to treatment are often due to an acid-fast infection.

Coupled with a suggestive history, one should have an appreciation of the pathology and the various localization sites. It is well known that adult tuberculosis is essentially an upper-lung disease; the number of cases of basal tuberculosis without upper-lobe involvement being comparatively small. The right apex is the usual site of the involvement, most frequently, 1 to 1½ inches below the apex, corresponding anteriorly to the middle of the clavicle. Extending from this point the process tends to spread backward and then downward in its typical "line of march" with the less denser involvement toward the base. A less usual site for the initial involvement is the first and second interspaces below the outer third of the clavicle. Secondary involvement in the lower lobe is also of great importance, for, although it follows upper lobe involvement, it may be far more extensive than the original focus. The apex of the lower lobe is the most usual site. As the disease progresses further the apex of the left upper and sometimes the left upper at a point corresponding to the middle of the axilla are involved. We must bear in mind that, while lues may simulate any type of lesion of tuberculosis, it more frequently involves the lower lobe. Upper-lobe pneumonia in adults, while it may be of the true lobar type, is frequently tuberculous in nature. Other conditions, such as mycotic infections and bronchiectasis, must be borne in mind. Malignant disease, too, may simulate the physical findings and history of far-advanced tuberculosis.

The statement can be made that the presence of persistently coarse, crackling râles in the upper half of the chest should be viewed suspiciously as the result of a tuberculosis process. However, a too great dependence should never be placed on physical examination alone as a "proof positive" of tuberculosis.

It is needless to stress the importance of sputum examinations. While occasionally upper respiratory involvement may give the tubercle bacilli in the sputum, it is generally accepted that a positive

report is conclusive evidence of pulmonary tuberculosis. Often an extensive lesion yields negative reports for a time and it is only after numerous examinations that a positive result may be obtained. Frequently a positive report is obtained only by guinea-pig inoculation. When we have a suggestive history and physical findings, with the presence of crackling râles, a persistently negative sputum report should cause us to look for other etiological factors in the production of this lesion.

The place of the *x*-ray in the diagnosis of pulmonary tuberculosis is very important. The *x*-ray is becoming a more important adjunct in our armamentarium, and we must take frequent recourse to its use. The *x*-ray cannot diagnose activity, although it can differentiate between an old lesion and one of recent occurrence. With the aid of the *x*-ray a definite lesion of a particular nature in the upper half of the chest may be revealed; in very early lesions, however, it is unfortunately of very little help. Frequently we receive a negative report and still have positive findings with positive sputum, and it is in these early doubtful cases where one needs the greatest assistance.

As is well known tuberculin is a concentrated glycerin broth upon which the tubercle bacilli have been grown for a given time and standardized in an arbitrary manner. For diagnostic purposes it is useful in infancy and early childhood. If the tuberculin test is done from a quantitative standpoint, there is a definite relationship between the activity and contact of an individual to the sensitivity and the degree of reaction. For example: If a person has an active lesion, or is in contact with a positive case, the intradermal reaction to 0.001 mg. of old tuberculin gives a 4+ reaction in a larger percentage of cases than it would in negative cases or the contacts of negative cases. On the other hand, a test with 0.1 mg. is often made before any reaction in negative cases or in contact of negative cases is shown. The severity of the reaction is judged by the degree of the edema, inflammation, local necrosis, vesiculation, lymphangitis and subjective symptoms. The value of tuberculin in diagnosis is of greatest service in children. Occasionally a positive far-advanced case of tuberculosis gives a negative reaction when complicated by measles or other exanthemata, pneumonia and cachectic conditions. The tuberculin reaction decreases in severity and sensitivity as the healing process progresses.

The complement-fixation test for tuberculosis is still in a state

of too great uncertainty to be used as a diagnostic means. Wassermann reports a rather encouraging series of results, but American experimenters have failed to substantiate these.

The erythrocytic crises of Fahreaus is of little value in diagnosis. He has noted that when citrated blood is permitted to stand, the rate of sedimentation of the erythrocytes varies in different diseases. He has noted that while the rate is greatly increased in active, far-advanced cases of tuberculosis, there does not seem to be any definite ratio established by which he can judge the degree of activity of these patients. He has noted that the velocity of this sedimentation is also increased in a great many other diseases, as lues, arteriosclerosis, chronic arthritis, psychosis and malignancy.

In considering the subject of treatment there is very little that is new. There are certain well-known practices however that seem to meet with success in the hands of a certain group of men who are doing their utmost to handle the problem successfully.

Undoubtedly, the first and by far the most important feature is bed-rest. The old idea of exercise, of going out into the woods and living a camper's life, or walking so many miles each day, of doing a certain amount of gymnastic work, has been replaced by the saner method of putting the patient to bed. This seems to be a most difficult problem at times; but all circumstantial difficulties must be disregarded and the patient placed at bedrest and kept there as long as there is any activity. By "bedrest" is meant leaving the bed only to go to the bathroom. "Bedrest" has proven to be the best adjunct in the hands of the majority of practitioners and should be persisted in as long as there is any activity present. What is meant by activity? It is generally accepted that activity is present when the temperature is above 99° F. for men and 99.4° F. for women; when the pulse ranges above 90, and when certain symptoms are present, especially hemoptosis, pleurisy or night-sweats. How long should the patient be kept in bed is the next question? This, of course, depends upon the severity of the infection and the length of time necessary to bring the temperature and pulse within normal limits. For example: If it requires a month of bedrest before normality is reached, it is well to keep the patient in bed for another week before beginning the "cure" treatment. On the other hand, if the activity is much greater, we would naturally keep the patient in bed two or three weeks at normal limits before permitting him out of bed. The following is the method used by Dr. Kaufman at the Rush Hospital:

The patient is started at a ten-minute interval out of bed, sitting in a chair. This interval is increased each alternate day by ten minutes, but resting in bed the intervening days. Throughout this period of cure, as it is termed, close observation is kept of any reaction as evidenced by a rise in the temperature or pulse-rate. When the patient's tolerance is increased to an hour and a half, we increase more rapidly—fifteen minutes every other day—until the patient is sitting up three hours. Then we increase by thirty minutes, and finally by an hour up to six hours. Sitting up six hours per day, plus the two hours of absolute quiet period that is insisted upon after the noon-day meal, make a full day. After cure for a week in this fashion the patient sits up two days and rests the third, for a week. This is so increased until the patient is sitting up every day all day.

In considering the question of exercise it must be realized that this varies with the facilities of the different institutions. Some have walks where the patient increases the walking period each day. Others have light tasks increasing in severity until the patient can tolerate a few hours of work each day, for example: beginning with five minutes the first day and increasing by five minutes every other day until one hour is reached. Then the patient is placed to work at light tasks.

While it is needless to stress the importance of fresh air, it would seem of value to say a few words about climate. Undoubtedly, a high, dry climate is the more ideal one for the average case. Whether it is merely a change of environment or the invigorating influence of the higher altitude is a matter for much debate. But, be that as it may, the average tuberculosis patient is benefited by the change to the mountains. As to the superiority of the West over the East, statistics show that the mortality rate is no greater in the East than in the West. There is no marked difference in the method of treatment or increase in the span of life in patients in either locality. Coupling these facts with the long, strenuous journey, the increased expense and the great distance from home should make one hesitate to recommend Western locations as a probable cure-all.

5. The dietary treatment of pulmonary tuberculosis is of extreme importance, inasmuch as the disease is of a progressively debilitating type and therefore the caloric intake must be maintained at a high level. The food must not only be easily digestible, but also very palatable: An abundance of milk, 6 to 8 glasses should

be taken, in addition to three meals a day. There is a great diversity of opinion as to the value of eggs in the tuberculous dietary. As many patients cannot tolerate this food product, we cannot rely too much on this substance to increase the food intake.

It is needless to stress the fact that all drug treatment is non-specific and only symptomatic. Such being the case, it is not necessary to reiterate the list of drugs that you have at your disposal to meet the various symptoms as they arise.

While tuberculin has some value as a diagnostic aid, its use as a therapeutic agent is discredited by the best authorities.

Pneumothorax is one of the newest aids in the treatment of tuberculosis. This procedure consists in the instillation of air into the pleural cavity, thus producing a collapse of the lung, which may be either partial or complete. By this method the affected lung is supposed to be placed at rest. The most ideal type of case for the employment of pneumothorax is (1) uncontrollable hemorrhage, which may at times prove rather difficult, owing to the difficulty in localizing the site of the hemorrhage. (2) One-sided lesions with slight or no involvement of the opposite lung, especially when there are no adhesions binding the diseased lung down to the pleura and so preventing a collapse. While these adhesions may prove a serious obstacle in the successful treatment, some report rather favorable results by the use of partial collapse on the worse side. (3) In very early cases where one lung is practically free from activity, and for which sanitorium treatment has not proved successful —that is, cases which, after three or four months' sanitorium treatment, continue to have evidences of toxemia, excessive cough, positive sputum, nightsweats and the like. These latter cases are usually improved after the first month of treatment.

The attitude of the patient to pneumothorax is usually enthusiastic, as would be expected for any treatment which causes the unpleasant symptoms to disappear and makes the patient feel better. Nevertheless, the virtue of this method of treatment is markedly curtailed—as great selectivity must be shown in the choice of cases; as even the supposedly ideal type of cases are handicapped by complications, such as pleural effusion, empyemia, pleural shock, air embolism and the necessity of continuous refills. Not only do the above-mentioned conditions occur, but occasionally a case may lie dormant for a year or more, when activity sets up in the opposite lung.

Until two years ago, heliotherapy in the treatment of pulmonary tuberculosis was done in a rather haphazard manner, without any definite uniformity of exposure, with the consequent rather discouraging results. At this time Rollier and later Lograsso began to systematize the time of exposure and the amount of surface exposed. They were so favorably impressed by the results in surgical tuberculosis that use was soon made of this method in the treatment of pulmonary tuberculosis in many of the sanatoria throughout the country.

The method is essentially that of increasing exposure each day of greater areas of the body until the entire body is exposed. For example:

On the first day the patient, reclining on the bed with eyes protected from the sun by means of colored glasses or towel and the head by a linen cap or bonnet, is taken to the sun porch. The only clothing worn are trunks. Only the feet are exposed and irradiated on this day. They are insolated for periods of five minutes three times during the day with intervals of about one hour.

On the second day each insolation period of the feet is increased to ten minutes and more of the body treated by insolating the lower extremity from the knees to the ankles for five minutes.

On the third day the feet were irradiated for fifteen minutes each period, the time of insolation from the knees to the ankles is increased five minutes, and still more of the lower extremity is treated by insolation by exposure from the hips to the knees for five minutes.

On the fourth day, the entire lower extremity is now receiving sunlight in the following doses: Hips to knees, ten minutes; knees to ankles, fifteen minutes; feet twenty minutes, and the abdomen is exposed for five minutes.

On the fifth day the insolation periods are, now, abdomen ten minutes; thighs, fifteen minutes; legs, twenty minutes, and feet twenty-five minutes. The last part of the body to receive its initial insolation, the chest, is now exposed for five minutes.

From this point each part is increased each day by five minutes until the twelfth day, when the feet receive an insolation of one hour three times a day. While the feet are maintained at one hour, the other parts of the body are increased until the entire body received three hours of irradiation per day. The anterior and posterior surfaces receive the same amount of irradiation, the total exposure being equally divided between both surfaces.

The pulse, temperature, respiration and, if convenient, the blood pressure are observed before and after exposure. Untoward reactions, such as fever, tachycardia, headaches, hemoptyses, etc., indicate an immediate cessation of the exposure, to be resumed at shorter intervals later on. Some observers claim that after a period of this treatment the condition of the patient changes, his morale improves and the symptoms seem to lessen. They report that as improvement increases the skin becomes tanned, softer and velvety in appearance; the patient becomes more robust, and there is an amelioration in symptoms and signs.

Artificial heliotherapy, while it falls short of the results obtained by natural sunlight, is a useful adjunct; it may be employed in extrapulmonary conditions, such as laryngitis, rectal fistula and fissure, nasal and ear conditions. It is also useful to keep the spirit of the patient buoyed-up on cloudy days or when natural sunlight is not available.

As is well known, there are advocates *pro* and *con* for sanitorium treatment of the tuberculous patient. Not all patients require sanatorium treatment. Most of the criticism is often due to the fact that physicians expect too much of a sanatorium. The patients at times are told that if they wish to get well they simply need to go to a sanatorium. The advice is excellent, although it is somewhat incorrectly expressed. It would seem far better if the statement were made that if they wish to begin to get well they should go to a sanatorium. If this thought is kept in mind, then, the sanatorium will not fall short in accomplishing its purpose. Six months to a year in a sanatorium rarely cures a case of tuberculosis. It is really a starting point—a railroad depot—from which the patient receives the directions toward the road to health. Primarily, it establishes a partial arrest of the disease. Secondarily, and probably of greater importance, it teaches the patient personal hygiene and proper care, so that he can maintain this arrest at home. Usually, when the tuberculous patient starts his treatment at home, instructions are carried out in a haphazard manner: routine is not appreciated; rules are distorted by the interference of well-meaning friends and relatives; there is never a deep appreciation of the importance of absolute obedience to a rigid régime. As the patient begins to improve, it is most difficult to keep him confined to bed, which is a rather simple matter at an institution. Taken all in all, our sincerest efforts are taken entirely too lightly, and the results

are most discouraging. It has been shown that twenty-five years ago the greatest death-rate from tuberculosis was between the ages of twenty and thirty years. Today it is between the ages of forty and fifty years, pointing out the fact that while tuberculosis is not being cured, twenty years of a more or less useful life are being added to the so-called curable cases. This is all done by merely aiding Nature with rest, feeding, fresh air, sunshine and proper regulation of their lives.

It is after a patient has received some sanatorium training that home treatment can be easily continued: the patient appreciates rest; realizes that exercise is not indicated with an increase of temperature and pulse-rate; that a limitation of activity is of paramount importance; teaches him personal hygiene, particularly as to the care and disposal of sputum, care of dishes, etc. E. R. Emerson states that the whole future of the consumptive depends upon a readjustment of his life, and weeks and months should not be wasted by a false start or delay in the course of instructions in the habits of living which must be maintained for months and years if permanent results are to be obtained. The patient will only begin to learn to properly readjust his life at a sanatorium.

In closing, an appeal is made for early diagnosis, not to wait for a positive sputum report or even for physical signs in the chest; again stressing the history of hemoptysis and pleurisy with or without effusion. When such a diagnosis is made, either tentatively or positively, have the courage of your convictions and send the patient to a sanatorium where they can learn to readjust their lives and so add fifteen to twenty years of usefulness.

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## Dental Infection and Heart Irregularities

BY S. CALVIN SMITH, M.S., M.D.
(By Invitation.)

(*Abstract*)

This paper is based on the theme that the relation between periapical infection and heart disturbances is an idea of recent origin, having first been introduced to the profession in 1910 by Sir William Hunter. Since that time dentists have made progress in their

handling of the subject, but the medical profession has been slow to grasp the relation between dental infections and heart conditions.

After enumerating the various causes of heart irregularities, Dr. Smith recited in brief the history of five patients in whom the removal of periapical abscesses was followed by a return to normality of a previously harassed and irregular heart. Electrocardiograms, showing the heart records before and after eradication of periapical abscesses, were used to illustrate the points under discussion.

The paper was summarized as follows:

1. Heart irregularities will sometimes disappear when peridental abscesses are identified and surgically removed.

2. The *x*-ray is of assistance in identifying peridental abscesses, but it cannot supplant thorough clinical examination and exhaustive tooth-vitality tests at the hands of a modern dentist.

3. A dentoradiogram that fails to show rarifactions should not lead the physician to absolve the teeth from blame when tracing the cause of heart abnormality. Clinical dental examination is necessary.

4. Should a dentoradiogram present suspicious rarifactions, the accused teeth should be subjected to a clinical dental examination.

5. A periapical abscess which is determined to be present by *x*-ray and by clinical studies admits of no compromise. That abscess should be surgically removed, even though the removal of the abscess means the removal of the tooth. It is unscientific to assume that an abscess can be "treated" through a small opening in a tooth and thus rendered harmless permanently. The physician who has charge of the health of a patient should not countenance such a temporizing maneuver, which is always inimical to and frequently jeopardizes the heart integrity of that patient.

6. The form of heart irregularity which occurs with the greatest frequency in association with periapical dental abscesses is the irregularity known as the premature systole. In the general run of patients who are concerned about their hearts, and who as yet are not in any sense cardiac invalids, the premature systole is the irregularity most likely to be present.

7. A study of the heart is incomplete without radiographic and clinical studies of the teeth.

MARCH, 23

## A Modification of the Urea-concentration Test

BY HAROLD W. JONES, M.D.

AND

A. CANTAROW, M.D.
(By Invitation.)

Many attempts have been made in recent years to develop a satisfactory test for the urea function of the kidney. Ambard presented his coefficient of urea excretion; F. C. McLean introduced the McLean index, which utilized the principles of Ambard's formula, but simplified them; H. MacLean and O. L. V. deWesselow brought out the urea-concentration test; Addis studied the ratio between one-hour urine-urea and the urea in 100 cc of blood, and Rabinowitz the urea-concentration factor $\frac{\text{Mg. urea in 100 cc urine.}}{\text{Mg. urea in 100 cc blood.}}$

Various investigators have shown that urea excretion in normal individuals depends on blood-urea concentration as well as renal efficiency, and also that the concentration of urea in the urine in normal persons can be increased indefinitely, under conditions compatible with life, by increasing blood-urea concentration. It has been further proved that the volume of water excreted has only slight effect on urea excretion when the blood-urea is not increased, and that when the blood-urea is increased the volume of water excreated that can influence the excretion of urea is between 2.5 and 6 liters; over this amount no influence is possible.

It is essential that a functional test be available as well as accurate in order that it may be useful. The urea-concentration test has enjoyed wide use in Great Britain. In this country its use has not been attended with success. The test is available for general use, but its accuracy must be questioned. The test, as described by MacLean and deWesselow, is as follows:

It is best performed in the morning. The patient is instructed not to eat after dinner the night before, so that the stomach may be empty. The bladder is emptied. The patient ingests 150 cc of water flavored with tincture of orange in which 15 gm. of urea have been dissolved. The urine is collected one and two hours

later, and if the second specimen is more than 150 cc a third-hour specimen is taken. The urea concentration is measured in the second- or third-hour specimen by the Marshall urease method. MacLean places the normal concentration at 2 per cent. A mild loss of function is indicated by a concentration of 1.8 per cent, and more severe grades by concentrations of 1.6 per cent or lower. MacLean states that this test yields a more accurate estimation of functional renal impairment than any other. E. Weiss found that the results paralleled those obtained with the phthalein test, and stated that it was valuable in the diagnosis of early nephritis.

Like most tests of renal function it fails in certain instances to denote accurately the degree of renal damage. This urea-concentration test often fails to give evidence of renal damage in the following conditions: In chronic nephritis with salt and water retention it is not uncommon to find a urine-urea concentration of 2 per cent or above; certain patients with symptoms of severe renal damage were studied in whom the urea concentration was 1.5 per cent or 1.6 per cent. The kidneys of these patients at necropsy showed almost complete loss of functionating tissue. The urea concentration should have been much lower. Not a few patients were seen with a high blood-urea whose urine-urea concentration was 2 per cent. Finally, any test in which the difference between abnormal and normal urine-urea varies only by 0.2 per cent must be open to wide possibilities of error.

We concluded from the results obtained with this test that in severe nephritis the urine-urea concentration would be almost the same following the ingestion of water alone as that following the ingestion of water plus urea. We felt that there must be a definite response of the normal kidney to the ingestion of urea and that a failure of response might indicate degrees of renal impairment. We termed the urine-urea concentration after water alone, "resting level," and after water plus urea, "urea response level." The following technic is used:

Instruct the patient to eat nothing after evening meal.

7 A.M. Ingest 150 cc of water.
8 A.M. Collect first specimen of urine.
9 A.M. Collect second specimen.
9 A.M. Ingest 150 cc of water flavored with tincture of orange, in which 15 gm. of urea are dissolved.
10 A.M. Collect third specimen.

11 A.M. Collect fourth specimen.

If fourth specimen is greater than 150 cc collect a fifth specimen.

Estimate the urea concentration in the second and fourth specimens by the Marshall urease method.

Ninety-three normal students and 30 patients with nephritis were studied by this method. The results of both the normal and the abnormal cases are divided into four groups:

1. Those with a resting level urea concentration, that following water alone, below 1 per cent.

2. Those with a resting level urea concentration between 1 per cent and 1.5 per cent.

3. Those between 1.5 and 2 per cent, and

4. Those with a concentration of 2 per cent or above.

*Normal Cases.* There are 25 in Group 1, with a resting level urea concentration of less than 1 per cent.

There are 31 in Group 2, with a resting level urea concentration between 1 and 1.5 per cent.

There are 28 in Group 3, with a resting level urea concentration of 1.5 to 2 per cent.

There are 9 in Group 4 with a resting level urea concentration of 2 per cent or above.

In Group 1 the resting level urea concentration and the urea response level urea concentration varies 245 per cent.

In Group 2, the percentage variation is 98 per cent.

In Group 3, the percentage variation is 47.8 per cent.

In Group 4, the percentage variation is 38 per cent.

In normal persons the lower the resting level urea concentration the greater the variation between it and the urea response level concentration. The higher the resting level the less the percentage variation between it and the urea response level.

The urea concentration is 2 per cent or above in all but eleven, following the ingestion of urea.

*Nephritis Cases.* There are 15 cases in Group 1; that is, with a resting level urea concentration below 1 per cent. The percentage variation between the resting level concentration and the urea response level is 66.5 per cent. In normal individuals it is 245 per cent.

There are 9 patients in Group 2; that is, with a resting level between 1 per cent and 1.5 per cent. The percentage variation is 25.5 per cent; In normal persons it is 98 per cent.

There are 3 cases in Group 3; that is, with a resting level of 1.5 per cent to 2 per cent. The percentage variation is 11 per cent. In normal patients it is 48 per cent.

There are 4 patients in Group 4, that is, with a resting level of 2 per cent or above. The percentage variation is 5.4 per cent. In normal individuals it is 38 per cent.

The degree of functional impairment may be proportional to the lessened amount of variation between the two levels.

Little variation between the two levels when the resting level concentration is high between 1.6 per cent and 2 per cent may be more indicative of renal impairment than a greater percentage of difference with a low resting level concentration.

In chronic parenchymatous nephritis the urea concentration may be 2 per cent or above, but the functional impairment present is shown by a percentage variation between the two levels that is less than normal.

Two patients may have concentrations between 1 per cent and 25 per cent. In one there may be considerable variation between levels, and in the other little or none. The one with the less variation has the greater functional impairment.

Functional improvement is shown by an increase in variation between levels in successive tests.

In those cases in which the phthalein test is between 45 per cent and 55 per cent the absence of normal variation between the two levels will denote the presence of functional impairment.

Discussion. This modification of the urea-concentration test is offered to remedy some of the fallacies of the test as heretofore described. The test is readily available and increases the accuracy of the interpretation of changes in urea elimination. If the urea-concentration test is to be used it seems better to consider the results from the standpoint of variation between a resting level urea concentration and urea response level concentration than from the urea concentration alone. This report does not include work upon any great variety of renal cases, and we are not able to state to what extent we may rely on lack of variation to indicate varying degrees of renal insufficiency. It seems to us, however, that the results obtained would indicate that this modification demonstrates with much greater certainty the presence of renal change in a given patient than does the old urea-concentration test.

Conclusions. Some of the fallacies of MacLean's urea-concentration test are discussed.

A modification of this test is offered in which the percentage variation between resting level concentration and urea response level concentration is shown to be more significant of renal damage than urea response level concentration alone.

Ninety-three normal individuals and 31 patients with nephritis have been studied. They are divided into four groups. Group 1 includes those with a resting level concentration below 1 per cent. Group 2, includes those with a resting level urea concentration of 1 per cent to 1.5 per cent. Group 3, includes those with a resting level urea concentration of 1.5 per cent to 2 per cent. Group 4, includes those with a resting level urea concentration of 2 per cent or above. Group 1 normals varied 245 per cent; nephritics varied only 66.5 per cent. Group 2 normals varied 98 per cent; nephritics varied only 25.5 per cent. Group 3 normals varied 47.8 per cent; nephritics varied 11 per cent. Group 4 normals varied 38 per cent; nephritics varied 5.4 per cent.

Functional improvement is shown by an increase in variation between the two levels when the test is repeated.

In some instances the phthalein test failed to denote the evident real impairment, yet the lessened percentage variation was comparable to the functional loss as indicated by physical symptoms.

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## The Unsuccessful Gastrointestinal Operation from a Medical Viewpoint

BY RUSSELL S. BOLES, M.D.
(By Invitation.)

*(Abstract)*

The literature abounds with evidence showing that the results of operation for chronic appendicitis, gastroduodenal ulcer and gallbladder disease are often disappointing. The reason operation fails to relieve symptoms is that the fundamental cause of the trouble

has not been discovered. Isolated pathology in one organ of the gastrointestinal system rarely occurs. Focal infection and biliary and intestinal stasis pave the way for the development of chronic gastrointestinal disease. In addition, such constitutional abnormalities as a disordered sympathetic nervous system, neurasthenia, cecum mobile, gastroenteroptosis, redundant sigmoid and familial predisposition are important etiological factors. The management of these cases before and after operation reduces itself to four main essentials: (1) Eradication of the foci of infection, especially those of the teeth, tonsils, sinuses, upper respiratory tract, appendix, gall-bladder and colon. (2) Elimination of intestinal stasis. (3) Elimination of biliary stasis. (4) Application of measures such as will improve the general condition of the patient. In a large proportion of cases in which therapeutic biliary drainage was employed, decided benefit was secured. In cases of intestinal stasis, properly performed colonic irrigation has given striking alleviation of symptoms in the majority of cases. In ileal stasis, transduodenal lavage, by the Jutte method, affords considerable relief. Diet is of paramount importance, one low in cholesterol being especially indicated in disease of the biliary tract. Only by such comprehensive management may recurrence of symptoms, reactivation or formation of ulcer, and recurrence of gall-stones be avoided. Operation in all such cases must be looked upon as only an incident in the treatment of the patient. The pathological conditions mentioned are frequently merely an end-result and surgery alone cannot be expected to effect a cure.

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## Artificial Light Therapy in Tuberculosis

BY EDGAR MAYER, M.D.
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(By Invitation)

The curative rôle of light in rickets and tetany is now commonly accepted. Under the influence of light the blood in rickets shows an increased phosphorus content, and calcium deposition in the epiphyses of the long bones readily takes place. The blood in tetany shows an increased calcium and phosphorus content and, clinically, the disappearance of such symptoms as carpopedal spasms, laryngo-

spasms and convulsions after a few exposures to quartz mercury vapor radiations. Lupus vulgaris of the skin is healed by combined local and general light exposures in almost 90 per cent of cases. Extrapulmonary tuberculosis in many forms yields to treatment with sunlight and artificial light radiations. These results have been so clear-cut in a large number of cases and yield so much promise that a knowledge of light and its clinical applications has become a requisite not only of the physiotherapist but also of the general practitioner.

My own use of light therapy, both clinically and in laboratory experiments, since 1917, and the noteworthy results attained by such practice have led to the presentation of this material. Because of the broad scope of this field of therapy only brief reference can be made to the more important facts.

Physical Characteristics of Light. A graphic representation of the divisions of the spectrum, showed the visible region limited on one end by the infra-red rays and on the other end by the ultraviolet rays. It may be convenient to recall that the visible spectrum extends from about 800 m$\mu$ to about 400 m$\mu$; the solar ultraviolet rays range from 400 to 290 m$\mu$, and the ultraviolet rays of artificial light sources from 490 to 185 m$\mu$. Those of a source such as the carbon arc have as their lower limit 220 m$\mu$, while those of the quartz mercury arc terminate at 185 m$\mu$.

Vibrations of all wave lengths appear to possess some light, heat and the ability to hasten or influence chemical reactions. As a rule, however, heat production is chiefly associated with the infra-red and the red rays; light is chiefly associated with the range from red to violet, while the most active rays chemically are the ultraviolet, blue, indigo and violet.

The infra-red rays are highly penetrative, while the ultraviolet rays possess this power only to a limited degree. The regions of the spectrum vary greatly in their degree of absorption in different substances. Water vapor, for instance, absorbs infra-red rays to a very great extent. Quartz and fluorite glass and clear distilled water are practically the only substances that do not absorb ultraviolet rays to a very great extent. Ultraviolet rays lose about 60 per cent in intensity in penetrating the atmosphere before reaching the lowlands. Ordinary window-glass absorbs ultraviolet rays below 330 m$\mu$. The ultraviolet rays between about 330 and 290 m$\mu$ are probably the best producers of pigmentation, and because o

their absorption by window-glass it becomes most difficult to tan behind glass, other than quartz. Snow, ice, water and sand increase ultraviolet intensity by reflection.

Photochemical Action of Separate Regions of the Spectrum. Infra-red rays produce an immediate hyperemia and redness, which, however, soon disappear after the cessation of irradiation. The deep penetration of these rays may cause deep heat action, although in guinea-pigs it has been shown that they are more likely to produce cutaneous blebs. The visible rays provoke light, heat and metabolic changes. However, the visible red (heat) rays are more likely than the infra-red rays to elevate subcutaneous temperature.

Ultraviolet rays are rapidly absorbed by most tissues to a depth, however, of approximately only 1 mm. and produce marked chemical or actinic changes in accord with Grotthus' or Draper's law, namely, that "only those rays that are absorbed can induce chemical changes." Hemoglobin quickly absorbs ultraviolet rays, as well as those of longer wave lengths, up to approximately 450 m$\mu$. Blood serum also absorbs the ultraviolet rays, chiefly because of its tyrosin and tryptophan content.

Action of Ultraviolet Rays on Protoplasm. The Brownian movement of colloidal particles quickly ceases on exposure to ultraviolet rays. Egg and serum globulin is precipitated at the expense of albumin. Lens-albumin previously sensitized by certain salts, such as calcium, sodium and magnesium, or by the silicates or dextrose, becomes susceptible to ultraviolet rays.

Bacteria are rapidly destroyed by these rays, the bactericidal effect becoming more marked as the wave length decreases. Temperature elevation increases this destructive action, while changes in the hydrogen-ion concentration appear to play no significant rôle.

Red blood cells *in vitro* are quickly hemolyzed, probably because of the destruction of the lipoidal membrane. This, however, does not occur *in vivo*. Protoplasm may be so affected by ultraviolet radiation, and thereby become especially sensitive to heat radiations.

A marked seasonal variation in intensity of solar ultraviolet rays exists, a phenomenon in some part correlative with the seasonal variation in the incidence of such diseases as rickets and tetany. There may also be a seasonal variation in the rate of animal growth.

The visible manifestations of tissue hyperemia due to ultraviolet radiation occur only after the lapse of a certain latent period (two hours or more). On repeated exposures, a product, melanin, is

formed in the basal cells of the epidermis. This may be due to the action of certain skin oxydases on a breakdown product of tyrosin, such as dioxyphenylalanin (Bloch).

Unicellular organisms are stimulated to certain physiologic changes, such as fission, or may be destroyed by ultraviolet radiation, depending on factors such as the intensity of the irradiation, the depth penetration of the wave length employed and the size of the organism. Thus, very short ultraviolet rays penetrate only to the cytoplasm, whereas longer ultraviolet rays reach the cell nucleus. Small doses of light appear to have a stimulating action, while larger doses produce deferred physiologic changes, and still larger doses may destroy such organisms.

The Physiologic Action of Light. Blood serum shows an increased calcium and phosphorus content under ultraviolet radiation in rickets and tetany. As a result there is an increased calcium deposit in the epiphyses of the bones in rickets, due in all probability to an increased absorption of calcium from the intestines.

Under solar radiation, the blood shows increased alkalinity, and this all the more under the action of the heat rays.

Animals kept in darkness from birth show no gross changes from those exposed to light, but blood examination shows a lower blood platelet count. On exposure of these animals to quartz mercury vapor radiations, the number of platelets is increased to normal.

Light exposures do not induce changes in red blood cells and hemoglobin, except a very transitory one, and this chiefly when a preexisting anemia occurs. Lymphocytosis in rabbits can be induced by exposures to the shorter ultraviolet rays. Cell membranes have shown an increased permeability on exposure to these short-wave lengths.

Basal metabolism is increased by light exposures alone, but this can be markedly increased by the additional action of moving air, winds and salt-water baths.

The rate of growth may possibly be increased under the action of light.

The Skin as an Organ. The skin may be considered an expansion of the nervous and circulatory systems. Its exposure to light rays produces an immediate and a delayed hyperemia, due either to the heat or to the chemical radiations. According to Krogh, the hyperemia induced by ultraviolet rays is caused by a direct action of the rays on the cutaneous capillaries. From an apparently life-

less, toneless and flabby skin, light exposures may produce a soft, velvety, colorful tissue. Under exposures to solar radiation, remarkable muscular tonus has been produced in unused muscles, despite prolonged application of immobilizing casts.

Increased physiologic action of the skin under light exposures may be predicated. Increased respiratory, excretory and protective power has been found to take place, and is now accepted as fact. It is rare to find acne developing in tanned skin. During an epidemic of chickenpox as Rollier's Clinic, no cutaneous vesicles were found on tanned skin, whereas they did appear on unexposed areas beneath plaster casts. Increased heat output by radiation under a provoked hyperemia must demand increased metabolism to supply the additional caloric output; this in turn may imply increased body metabolism. Under light exposures, respiration is decreased in rate but increased in depth. Increased body heat production obviously demands accelerated vital reactions.

The possibility of stimulation of the skin to produce so-called "antibodies" cannot be entirely discarded.

The action of light in the depths is in all probability an indirect one, by way of the nerves and the bloodvessels. The ultraviolet rays are absorbed by the epidermis; however, they may possibly reach the projecting capillaries of the dermis. The deeper penetration of the longer visible and the infra-red rays may allow of slight direct depth action, but there is little cause to believe that this can be of much therapeutic value directly.

Quartz Mercury Vapor and Carbon Arc Lights. Enthusiasts for heliotherapy insist on the use of radiations having a spectrum closely resembling that of sunlight. There is no other basis for this than that the results with solar exposures have been most favorable in the hands of these workers. There are sufficient grounds for expecting therapeutic results with other combinations of light rays. We may logically reason that certain diseases are more easily responsive to sources of greater intensity in ultraviolet radiation than to solar radiation. Empirically, this has been noted in the treatment of certain forms of tuberculosis.

The quartz mercury vapor light has a preponderance of the short ultraviolet rays, but also emits the longer ultraviolet rays, the blue, indigo and violet rays, and some few green and red rays. Heat particularly comes from the heated mercury and tungsten electrodes, the quartz container and the reflecting hood.

The carbon arc emits wave lengths similar to those of sunlight, but with a preponderance of infra-red and longer ultraviolet rays.

Clinical Observations. Only brief reference may be made to the use of light, more especially the mercury quartz, in a few major complications of tuberculosis.

*Intestinal Tuberculosis.* The diagnosis of intestinal tuberculosis is, as a rule, established by the subjective symptoms of alternating constipation and diarrhea, vague digestive complaints, abdominal pain, nausea, vomiting and soft or watery stools; or merely by persistent loss of weight or slight elevation of temperature, otherwise unexplained, or by any or all of these symptoms combined with roentgen-ray demonstration of filling defects in the cecum or ascending colon (found in a case of pulmonary tuberculosis).

An *x*-ray picture taken before treatment, showed this defect in the cecum of a patient suffering from intestinal tuberculosis, and another film showed its complete disappearance after eight months of quartz mercury vapor exposure; this was accompanied by a complete cessation of digestive complaints. We are convinced, after the study of a large series of patients so treated, that this is not merely a spontaneous recovery but one directly influe ced by the treatment employed. Too many cases have now been seen (eighty-eight of them I have rather carefully studied and a larger series has been reported by others, such men as Brown, Stewart and Pritchard) to conclude that the benefits were the result of mere coincidence. Experimental studies are now in progress at the Saranac laboratories which aim to elucidate the mechanisms involved.

*Hilum Tuberculosis.* A type of tuberculosis in which it appears that the importance of the favorable influence of light action has not been sufficiently stressed is hilum tuberculosis. If the roentgen-ray and physical examinations reveal no definite pathologic conditions, then the diagnosis is necessarily made a method of elimination in children or adults having some form of combination of symptoms, such as elevation of temperature, tachycardia, loss of weight, strength and appetite, or cough and expectoration together with a marked sensitiveness to tuberculin inoculation. I obtained especially favorable results on application of mercury quartz radiation in the majority of 18 such cases in which combined therapeutic measures without light had previously failed, and a direct relationship between the treatment employed and the clinical effect had to be concluded.

*Superficial Tuberculosis.* To study the effect of light exposures on superficial tuberculosis, we produced an experimental bovine tuberculosis of the cornea in rabbits and then irradiated these with mercury quartz light alone or in combination with certain sensitizing substances, chiefly dyes, directly applied to the lesion. Variations in response occur with different exposures and the different sensitizing substances employed.

*Lupus Vulgaris.* Lupus vulgaris and ulcerative tuberculosis of the mucous membranes, such as the pharynx, respond to combined local and general body exposures. The possibilities of affecting a laryngeal tuberculosis with artificial light sources are theoretically promising, since it is possible to provoke chemical changes of tissue, focal reactions (as with tuberculin treatment), hyperemia, and even destruction of at least the most superficial of the bacteria. The hyperemia may induce an analgesia in painful laryngitis. We are now using a special form of water-cooled mercury quartz light, applied directly to the larynx, both alone and in combination with sensitizing substances, such as eosin and quinine. The results are promising, particularly when focal reactions are induced, but they do not yet permit of conclusive deductions.

It seems imperative in all forms of tuberculosis to which light is applied to combine both general and local irradiations. It has been shown that healing takes place in 30 per cent more of cases of lupus vulgaris when general body irradiations are used in addition to local exposures.

Conclusion. Lack of time precludes the consideration of other important complications of tuberculosis, such as bone and joint, peritoneal, fistulous and glandular. Light may be particularly advocated as an adjuvant in these types of cases.

Reliance on its use in pulmonary tuberculosis is not to be especially encouraged.

Other factors, such as pigment, its formation and function, the matter of dosage of light application and the mode of light action, cannot be entered into here. This presentation has been made chiefly to hint at future possibilities of light therapy which will require closer coöperation between clinician, laboratory experimentalist and physicist.

APRIL 27

## The Ambulatory Care of Diabetic Patients

BY RUSSELL RICHARDSON, M.D.

The care of ambulatory diabetic patients differs very much from that of patients in the wards. The physician has complete and accurate control of the ward patient's diet, the most important single factor in the care of these cases. The patient must eat what the dietitian serves him and he can rest secure on the dietitian's measurements, variety and preparation of his food. In addition, the physician sees him daily, or more often if necessary, and can easily change a line of treatment which he finds unsatisfactory. The dispensary patient, on the other hand, must be his own guide, philosopher and friend in all of these matters. He must voluntarily keep within the regulations which we have set for him and must use his own discretion in following our directions. Moreover, in giving him directions, we must bear in mind that he is limited in his facilities for carrying them out, and that, as we see him only at intervals, we must give him directions which will not lead him into trouble between visits. To help him over these difficulties there should be close coöperation between doctor and patient.

There is no disease in which it is more necessary that there be a clear understanding between the patient and his physician. So much of the value of the treatment depends upon the attitude of the patient and the care and thoroughness with which he follows instructions. The treatment itself is largely simple diet regulation and there is little of medicine or other forms of therapy to impress the patient. It takes real faith in the doctor to make many patients believe that the difference between good health and poor health, for them, lies in eating spinach instead of potatoes. How many times have we seen patients who have been on a diet for a long time and yet have no real conception why? And when full explanation was made to them of their condition and the vital necessity that a diet would always be to them, they have readily adopted it as an integral part of their lives.

The patient should be very frankly told that he has the choice of keeping well by means of diet, with or without insulin, or of

continuing his present full eating with illness of some form looming over him. There seems very little to be gained and much to be lost by failing, at the beginning, to impress him fully with what he must expect. If it is a shock to him at the time, he soon recovers mentally, following the physical improvement which accompanies the decrease in blood-sugar. As he receives more to eat, with especial care as to his likes and dislikes, he finds that even a diet is not so bad as he had anticipated. In this preliminary talk he should be strongly impressed with the fact that the gland, which is damaged, needs, most of all, rest, just as an overworked heart or other organ, and that he can best give it this rest by following our directions and diets.

In making up diets for our patients perhaps we cannot do better than keep in mind what have been called the four principles of the diabetic's diet. These deal with total nutrition, carbohydrate, protein, and the carbohydrate fat ratio. First, we must never forget that, if the diabetic is to be a useful member of his community, he must have enough nourishment to conserve his weight and strength to the end that he may fulfill his daily tasks. Living on a diet that barely keeps body and soul together leaves him with no energy and an easy prey to all infections. On the other hand, overfeeding quickly increases his weight and his rate of metabolism, and, in so doing, adds to the severity of his disease.

Second, the carbohydrate fraction of his diet is set for us by his tolerance. There is nothing to be gained by feeding carbohydrate which cannot be metabolized and must only accumulate in the blood and tissues. And yet the carbohydrate part of our diet is such an important part, that the patient will live the happier the more carbohydrate we can let him have.

Third, the protein, which used to be the mainstay of the diabetic diet, we now know should be relegated to its own sphere of supplying nitrogen for the body tissues. One gram per kilogram of body weight per day suffices for this and more than this amount merely adds to the metabolic rate and causes trouble.

Fourth, the ratio between the fat and carbohydrate which we can use is now much better understood than it was even a short time past—thanks to a long line of investigators. The outcome of this work is our present knowledge that, if we keep the fatty acid forming part of the diet down to one-half again as much as the carbohydrate portion, we will have no danger from the formation of $\beta$-oxybutric

acid. This ratio can be increased somewhat without there being danger from acidosis.

In making up our diets, if we give 1 gram of protein per kilogram of body weight and the tolerated amount of carbohydrate, it is evident that we must get the remainder of the calories from fat. This fat can come from either the food or the tissues. If it comes from the tissues we must not lose sight of its presence and be sure that there is sufficient metabolizing carbohydrate to take care of it. It is well known now that body fat will be burned before protein to provide the required calories, and, if there is no body fat to be spared, that protein will be used. Of course, if much protein is used in this way, there will be a large amount of sugar released from it for the body to burn. This may, in very thin persons on a low diet, reach 200 grams per day, a large amount for a diabetic to metabolize.

In carrying out the treatment we use, in the Metabolism Clinic of the University Hospital Dispensary, a series of four diets of a carbohydrate content of 27, 51, 78 and 104 grams, a fairly constant protein of about 60 grams, and sufficient fat to make the calories total 853, 1350, 1960 and 2450 grams per twenty-four hours. The total carbohydrate of these diets is 62, 93, 126, and 156 grams respectively. In using these diets we do not expect to bring patients of many weights and ages to the same caloric intake. We do, however, feel that we materially reduce the work and simplify the technic of diet care. It is not at all difficult to alter these diets by means of bread, butter and eggs, in order to change the amounts of carbohydrate, fat and protein. The diets are made up of simple foods, and in this way, perhaps, fit well into the lives of dispensary patients. The measurements are by such simple home methods as the tablespoonful.

I might stop here for a moment to speak of the so-called diabetic foods, most important of which are, of course, the breads. The flours used in making these breads generally have a high-protein content which, with the eggs used in the making, gives a food the protein percentage of which is out of all proportion to its value or palatability. When we remember that 58 per cent of all protein is transferred over into carbohydrate in the body, it is evident that we are giving almost as much carbohydrate as we would give in white bread. In addition we must greatly increase the protein ration or else cut down on the meat, eggs, cheese and other more

palatable and useful foods of that class. We feel that patients do much better to use a bran biscuit of no food value at first and gradually change over, if they improve, to small slices of whole wheat bread. There has recently been put on the market a flour which has almost no food value and which with care will make a fairly satisfactory low-calorie biscuit. This, however, is expensive for the dispensary patient.

As you know, it has come to be the custom in many clinics to try to teach the patients to make up their own diets and to examine their own specimens for sugar. Our experience has definitely led us to the opposite point of view. We find that many patients, when they examine their own urine, are apt to be continually experimenting with their diet, apparently feeling that, if they have no sugar in the urine, they are not taking as much carbohydrate in the diet as they might. Consequently, in trying to increase their food, with the urine as a guide, they have sugar much of the time. Sugar in the urine, meaning as it does an increased blood-sugar, we believe, should never be countenanced in a patient even in small amounts. A patient who is allowed to have a little will soon be having a large amount, with the consequent strain on the pancreas.

As regards the making up of their own diets, by figuring in grams and calories, we have found that the class of patients with which we deal have great difficulty in learning this and that most of them prefer to accept from the dietitian a complete diet with a list of substitutions, which they can use at will. Moreover, we have in the clinic, during the college year, third-year medical students. These men, we have found, can grasp the essential points of diabetic treatment, during the time they are with us, when based on standard diets as a foundation, but have considerable difficulty in acquiring the detailed knowledge of foods necessary in order to make up well-balanced diets alone. Some form of standard diets of this sort should also be an aid to the general practitioner, who does not have a sufficient number of diabetic patients to justify him in trying to keep at his finger tips the varied knowledge of the dietitian.

When first seen, in order to get rid of the excess sugar, which is generally present, we place the patient on the lowest diet of 853 calories, unless there are contraindications to this proceeding. He is told to return in two or three days. He receives a careful explanation of any points which are not clear to him. If the patient returns sugar-free at the next visit, we increase the diet, step by step, at

intervals of a week, until he is holding his weight and strength, and still remains sugar-free. Up to this point we have not allowed him to have any great variety of food, feeling that until he becomes accustomed to the diet, the more simple it is the better. When, however, he has become sugar-free and is holding his weight and strength for a time, we begin to allow him to substitute for parts of his diet other things of equal value, in order to add variety to his daily ration. As it is so easy for a diabetic, not under observation, to become lax about his diet, we insist that the patient shall report to us monthly, for checking up blood and urine examinations and for further diet instruction.

If it appears that our patient, at any stage of his care, cannot become sugar-free on any diet, or cannot hold his weight and strength on any diet on which he can remain sugar-free, he is advised to take insulin. When this valuable aid was first introduced it was so unstable and so unstandardized that hospitalization was necessary, and it is still desirable that all patients who are severely ill or who have one or another of the complications of diabetes, should begin with hospital treatment. However, there are not hospital beds enough in the country to accommodate all of the diabetic patients, and in addition, many people who are living lives of misery as a result of this disease cannot, for one reason or another, leave home or work for the days or weeks necessary to hospital care.

It has been our practice to divide patients, as regards taking insulin, into three classes, viz.: those who can take 125 grams of carbohydrate in addition to 50 or 75 grams present in the protein and fat in twenty-four hours, and who therefore do not require insulin; those who must take less than 65 or 70 grams of carbohydrate besides that in the protein and fat, in order to remain sugar-free and who should therefore have insulin to aid them in metabolizing a maintainance diet; and lastly, the middle group between these two. The taking of insulin by this group, we believe, should be governed by accompanying factors, as whether they can afford it, whether they need a larger diet to carry on work, or whether they are sufficiently fond of starches to make the insulin a small price to pay for them. That is decided after a personal talk between patient and physician.

Realizing the necessity of avoiding excessive sugar on the one hand and shock on the other, we have finally chosen the following

routine method of proceeding with insulin treatment for a patient in the dispensary: After several days on the lowest diet of 853 calories has shown his inability to become sugar-free, we place him on a diet approximately basal in amount with 50 grams carbohydrate, and give him 10 units of insulin once daily. The basal diet for so many of the patients runs about 1300 calories that we have come to use the No. 2 diet very frequently. The insulin is given by the dietitian for several days with careful instructions to the patient until the latter soon finds that it is not so difficult as he thought, and that by following instructions he is able to do it for himself at home before breakfast. We have used this method now for eighteen months and have yet had neither infections nor severe shocks in any patient. After keeping this diet and insulin for several days, or until there is no further change in the amount of sugar excreted, we gradually increase the diet or insulin, as indicated, by increments of 5 units of the latter and 10 grams of CHO, with accompanying fat increase, until we have a palatable maintenance diet which can be held without excreting sugar. When the patient has become stable on this combination, a blood-sugar tells us if our result is satisfactory. This diet and insulin we note as a standard to which we can return at any time in the future after a period of difficulty, or to find out if our patient has lost any tolerance.

All severe complications of diabetes such as infection or acidosis we send into the hospital immediately. We feel that nothing is to be gained by attempting to handle them in the dispensary, and that much valuable time may be lost. The presence of diacetic acid, which is looked for routinely in every urine specimen, is taken as a signal that trouble may not be far off. When this reaches what might be called + +, using ++++ as a typical strong reaction, the fat in the diet is cut to half or less, insulin is given, and the patient is told to return to the clinic daily until the danger is past.

Before closing I must speak of the service of the dietitian. The dietitian is almost the heart of a metabolism clinic, and if the training of social service worker is combined with a knowledge of dietitics we have a person who is invaluable to the clinic. We have, at the University, built up our clinic with this service. The dietitian, trained also as a social worker, is familiar with the home lives of the patients. She not only helps the patients after the manner of the regular social service, but she carries her diet work into the home. She is able to straighten up many problems of diet and insulin at

home, and is a special help to the medical staff in all cases where we suspect that the patient is not playing fair and keeping his diet. A visit by her and conversation with other members of the family often result in giving us information of much value in aiding the patients.

To summarize, our experience has definitely led us to believe that:

The patient must be taken into our fullest confidence in order to gain his coöperation.

He should always be sugar-free, not even a trace being allowed knowingly.

He must be on a measured diet, but measured by simple home methods.

He should not examine his own urine except in exceptional cases.

The dietitian should combine with her knowledge of diets, a thorough training as a social service worker to be of greatest service to the dispensary patient.

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## Results in the Treatment of Early Syphilis

BY J. E. MOORE, M.D.
BALTIMORE, MD.
(By Invitation.)

(*Summary, Paper No.* 1)

1. We present a plan of treatment for early syphilis, the essential features of which are:

(*a*) That treatment shall be continuous, consisting of courses of arsphenamine alternating with courses of mercury by inunction (or of insoluble bismuth salts intramuscularly), plus potassium iodide.

(*b*) That treatment shall be carried out under detailed serologic control.

(*c*) That treatment shall be prolonged without intermission for one year after the blood and spinal fluid have become and have remained completely negative.

2. Certain reasons attending the adoption of these standards are discussed.

(*Summary, Paper No.* 2)

1. We report the clinical results of treatment in 402 patients with early syphilis, of whom 42 had seronegative primary, 61 seropositive primary and 299 early secondary syphilis.

2. In this study a patient is regarded as probably cured if he is reinfected, or if a complete survey including physical examination and tests of the blood and spinal fluid, carried out at least one year after the date of the last treatment, show no evidence of syphilis. About one-half of our presumably cured patients have been followed for more than three years of probation.

A patient with a clinical or serologic recurrence of any type occurring during or subsequent to treatment is classified only with treatment failures.

3. Using a system of continuous treatment with alternating courses of arsphenamine and mercury, the probability of cure is in direct proportion to the duration and regularity of treatment. Only 10 per cent of those patients receiving eight or less doses of arsphenamine without mercury were cured; when two courses of arsphenamine plus interim mercury were given, 37 per cent were cured; after three courses, 56 per cent, and after four or more courses, 78.8 per cent of probable cures were obtained.

4. The optimum amount of treatment for early syphilis, with the plan advocated, appears to be a full year of treatment after the serology of blood and spinal fluid have become and have remained negative, excepting only seronegative primary syphilis, where a three-course treatment, lasting nine months, apparently produces satisfactory results.

5. Grouping together coöperative and uncoöperative patients, without regard to the character or duration of treatment, it is shown that if treatment can be begun within the first two weeks of the infection (seronegative primary syphilis), the chance of ultimate cure is almost twice as great as when it is delayed until the appearance of secondary manifestations. In particular, the incidence of reinfection in the groups of seronegative and seropositive primary and early secondary syphilis is 11.0, 8.1, and 3 per cent respectively. The extreme importance of early and accurate diagnosis is thus emphasized.

6. With the utmost coöperation on the part of the patient, and painstaking treatment and follow-up on the part of the physician,

it appears possible to cure 100 per cent of patients with seronegative primary syphilis, but only 80 to 95 per cent of those with seropositive primary or early secondary syphilis. The refractory 5 to 20 per cent seem likely, in spite of the utmost efforts of therapy, to develop late syphilis, especially neurosyphilis.

7. A comparative study of the results obtained from our plan and from the abortive system of treatment in vogue in Europe suggests modifications of our treatment system, which we discuss, although essentially similar results have been obtained from the two methods.

8. The recurrences observed in our material, classified into the groups of recurrent secondary syphilis, neuro-recurrences, tertiary syphilis, late central nervous-system syphilis and Wassermann-positive latent syphilis, are described and analysed in detail as to the amount of treatment received and the interval between treatment and clinical or serologic relapse.

9. Recurrences seriously impairing efficiency or endangering life (neuro-recurrences, tertiary syphilis, neurosyphilis) occurred in almost one-half the patients receiving eight or less injections of arsphenamine; in one-third of those receiving from one to two courses of arsphenamine plus mercury; in a one-quarter of those receiving three treatment courses; but in only 3 per cent of those patients receiving four or more arsphenamine courses plus mercury. The necessity of long-continued treatment is thus emphasized.

10. The tendency of inadequately treated syphilis to repeated relapses in the same patient is pointed out.

11. The short average time interval (2.1 months) between the date of the last treatment and the onset of neuro-recurrences emphasizes the necessity of continuous treatment in early syphilis.

12. Cardiovascular syphilis, especially aortitis, was the most common type of late recurrence observed.

13. Twenty-seven patients developed neurosyphilis, usually of the diffuse meningovascular type. The relative infrequency of general paresis (4 cases) and of tabes dorsalis (no cases) is explainable on the basis of the short period of years covered by this study.

14. The evidence of repeated routine spinal punctures in 54 patients permits the general statement that in early syphilis, if the spinal fluid is normal after six months' treatment, the patient will not develop clinical neurosyphilis or a subsequently positive spinal fluid unless a second redissemination of organisms (clinically mani-

fest by recurrent secondary syphilis or a recurrent positive blood Wassermann) occurs.

15. Periodic reëxamination from physical and serologic standpoints are absolute essentials in the evaluation of treatment results. Even though prolonged observation makes cure seem almost certain, a syphilitic patient should never be released from the obligation of periodic reëxamination throughout his lifetime.

(*Summary Paper No.* 3)

1. A statistical method is described which permits the charting of the average blood-Wassermann response to treatment of a large series of syphilitic patients.

2. This method is applied to 879 cases of early syphilis; and charts and tables are presented to show the response of the Wassermann reaction to treatment in 110 patients with seronegative primary, 151 with seropositive primary and 618 with early secondary syphilis.

3. In approximately 85 per cent of all cases of seropositive early syphilis a negative blood-Wassermann reaction may be obtained by a six- to eight-injection course of arsphenamine.

4. The composite Wassermann curve of patients under prolonged continuous antisyphilitic treatment is presented.

5. Composite curves of patients treated continuously are compared with those of a similar group treated intermittently, periods of treatment alternating with periods of rest. It is shown that from this standpoint continuous treatment is productive of greatly superior results.

6. An attempt is made to correlate this serologic data with the ultimate clinical outcome. From this standpoint, also, continuous treatment produces better results than intermittent treatment.

7. It is shown that in a certain number of patients with early syphilis the response of the blood-Wassermann to treatment may be, as compared with the average, abnormally rapid or abnormally delayed. Curves are presented to show these variations from the average.

8. An analysis of the material suggests that frequent repetition of the Wassermann test during treatment is of considerable prognostic value. Data are provided which further suggest that a "prematurely negative" Wassermann test may indicate a lack of resistance to syphilitic infection on the part of the patient.

9. A study of seronegative secondary syphilis leads to this same tentative conclusion, and indicates that a negative Wassermann in untreated secondary syphilis is an index of lack of resistance.

10. The applicability of the composite Wassermann curves to the problem of the provocative Wassermann reaction is pointed out.

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## Beriberi from a Diet of Raw Starch

(From the Neurologic Service of Dr. W. G. Spiller, Philadelphia General Hospital.)

BY E. J. KEPLER, M.D.
(By Invitation.)

Beriberi is seen so infrequently in the United States that its occurrence is worthy of mention. Cases of the disease do occur from time to time, but chiefly among the crews of vessels landing in our ports or among the Orientals. Vedder[1] has shown that the disease has been fairly common in our asylums and penal institutions, and since the publication of his work epidemics in prisons have been reported by both Travis[2] and Livengood.[3] Sporadic cases occur from time to time, but they are exceedingly rare, especially in this part of the country. The probable reason for our fortunate freedom from the disease lies in the fact that even in our lowest social strata the standards of living are sufficiently high to prevent its occurrence.

The etiology of beriberi is now generally accepted to be a deficiency in the diet of a specific vitamine known as water-soluble B. In eastern Asia this deficiency is usually the result of the excessive use of polished rice. On board ship, as Holst[4] has shown, vitamine deficiency results from the too exclusive use of canned foods and white bread. How the absence of the vitamine produces pathologic effects is not fully understood, but it seems likely that the vitamine is necessary for the proper metabolism of carbohydrates. Cooper and Braddon[4] pointed out that in birds a quantitative relationship exists between the amount of carbohydrates eaten and the amount of vitamine necessary to prevent the occurrence of polyneuritis; and Vedder[4] and Clark[4] have shown that if birds are fed on a total beriberi diet for only one week, characteristic microscopic changes

appear in the peripheral nerves; whereas birds fed nothing but water live three or four weeks and at the end of that time show no microscopic evidence of neuritis. To make this point clearer, an analogy between beriberi and diabetes might be drawn. In diabetes, a definite amount of carbohydrates must be metabolized to prevent acidosis. To prevent beriberi, a carbohydrate diet must be supplemented with a definite amount of vitamine substance. In other words, the water-soluble B vitamine is to carbohydrate metabolism what glucose is to fat metabolism. When the disproportion between the carbohydrate and the vitamine is not great, years may elapse before the onset of symptoms, which even then may be mild in character; but on a total beriberi diet pronounced symptoms occur after about ninety days.[5]

Because of the rarity of the condition, it might be well to review the chief features of the disease. In the fatal cases the pathologic findings are fairly constant and consist, first, in degenerative changes in the entire nervous system, but with the greatest involvement of the peripheral nerves; second, in dilatation and hypertrophy of the heart, with the microscopic evidence of degeneration, such as brown atrophy, edematous infiltration, vacuolation, fatty changes and sometimes even fragmentation and segmentation of the muscle; and finally in a generalized tendency to edema and effusions into the serous cavities. The changes in the other organs are not characteristic.

The symptoms are determined by the pathologic findings outlined above. In the mild cases the onset is insidious, with weakness, pains, paresthesias and finally paralyses of the extremities. Generally the legs are first affected. Along with the neuritic symptoms, the evidence of myocardial injury becomes apparent and the patient complains of palpitation, dyspnea, and precordial and substernal pain. Slight edema of the feet and ankles may appear. In this stage the disease may remain chronic for many years with slight remissions and exacerbations, but it may become acute at any time with collapse, general anasarca and death. Other cases go on to a chronic neuritis and flaccid paralysis without any edema. An acute form in persons apparently well occurs in which edema and cardiac failure predominate. In these cases death may occur in a few hours, or, if immediate recovery ensues, the disease may go on to the chronic atrophic type indistinguishable from those cases in which the onset has not been so spectacular.

The physical findings are those of a multiple neuritis, with or without edema, and cardiac failure. The heart findings vary greatly. Pulsations in the neck and epigastrium are common. There is practically always an enlargement of the heart to the right and sometimes to the left. The pulse is rapid, and there may be marked arrhythmias. The blood-pressure is usually described as being low, but in the 21 cases reported by Travis,[2] the systolic readings were uniformly high and the diastolic readings unusually low, the average pulse-pressure being 105.

Eye changes occur frequently, as shown by Fernando[6] and others. These include dimness of vision, disturbance of color sense, inconstant hyperemia, blurring of the optic disk and a slight neuroretinitis.

There are no constant laboratory findings. The blood usually shows a secondary anemia and variable changes in the differential picture. The urine is usually diminished in amount and only occasionally contains albumin; casts are rare. Few studies in the chemistry of the blood have been made. Arima,[7] in 1917, reported a moderate increase in the nonprotein nitrogen of the blood comparable to that occurring in chronic parenchymatous nephritis.

The prognosis, except in the acute cases in which death is the rule, is generally good. In some epidemics the mortality rate has been above 50 per cent and in others as low as 3 per cent. Conservative estimates place the average mortality at 5 per cent.[1]

Report of Case.—*History.* M. R., a colored woman, aged twenty-eight years, married seven years, had one child, aged five years, and had had two subsequent miscarriages. She was admitted to the Philadelphia General Hospital, October 18, 1924, and assigned to the neurologic service of Dr. Spiller, to whose courtesy I am indebted for the privilege of reporting this case.

Before the onset of the present illness, her health had been good except for influenza, in 1918, and occasional mild attacks of tonsillitis. In August, 1918, she had a miscarriage followed by severe vaginal bleeding. One of her friends recommended raw starch as a therapeutic measure. Acting on this advice and later influenced by a superstition among negroes that raw starch has cosmetic value and tends to make the skin white, she gradually acquired a fondness for this type of food, and would eat it from the box, piece by piece, as one would eat candy. At the end of two years this habit had increased to such an extent that she was consuming one of the popular brands of gloss starch in amounts ranging from 1 to 2 pounds (0.5 to 0.9 kg.) daily—approximately from 1600 to 3200 calories. Her husband ate only one of his daily meals at home, and rather than cook for herself she obtained most of her nourishment from the uncooked starch. The cooked meal at

night consisted of the usual staple articles of diet found on a working man's table. Under this regimen she lost her appetite, and as a result she practically subsisted on laundry starch, which, so far as its vitamin content is concerned, is certainly the equivalent of decorticated rice. The hold which this habit had obtained on her can be realized from the fact that on several occasions after her admission to the hospital she asked the nurses to smuggle starch to her. No other peculiarities or excesses in her habits could be discovered. Alcohol was ruled out by repeatedly questioning the patient, her husband and her neighbors.

In spite of her starch diet from August, 1921, she remained in fairly good health until May, 1924, when she began to notice unusual sensations in her hands and feet. She felt as though pins and needles were being stuck in her extremities and that insects were creeping up and down the legs. At times there was a transient edema of the feet. A little later she began to have a constant dull ache in the calves and severe shooting pains down the legs. At the same time she noticed that her extremities were becoming weak, and that she was short of breath on exertion. By September 1, there was marked edema of the feet, pronounced dyspnea on exertion, and sufficient loss of power in the legs so that walking became very difficult.

About the middle of September she consulted a physician, who within a period of two weeks gave her six intravenous injections of a yellow solution. This we thought was arsphenamine, but on subsequent investigation we learned that it was a preparation of calcium containing about 0.1 per cent of free iodine. Following this treatment she became much worse. Her vision failed rapidly, so that in two weeks she was almost blind. She became drowsy and subject to dizzy spells. She lost all sex desire and at the same time was troubled with an intense pruritus vulvæ, both of which symptoms she lamented very bitterly. There were attacks of severe substernal and abdominal pain with loss of appetite, nausea, vomiting, palpitation and dyspnea. There were no urinary disturbances other than that the urine became scanty and highly colored. The remainder of the history was negative.

*Examination.* On admission the patient, well developed and overnourished, was retching and vomiting. The temperature was normal, pulse-rate 120, and respiratory rate 35. She appeared to be very ill.

The vision of each eye was greatly impaired. She was able to recognize a hand passed before the eyes, but was unable to count the number of fingers held before her. The pupils were round and regular, with only a partial response to light. The fundi showed some pallor of the temporal sides of the disks, full veins, pulsating arteries and several recent retinal hemorrhages lying close to the disks.

The thyroid was palpable, but not tender. The lungs were normal. The cardiac impulse was diffuse and pounding, so that the left breast shook with each beat. Marked pulsations were observed in the suprasternal notch, over the carotid and temporal arteries, as well as over the abdominal aorta. There were vibratory thrills felt at the base of the heart and in both carotid arteries. The heart was enlarged to the right and to the left, as shown by the teleroentgenogram (Fig. 1). The heart sounds were of

a poor quality, the rate accelerated and the rhythm normal. Three distinct murmurs could be heard. At the apex there was a soft, blowing, systolic murmur and at the base to the left a very loud, rough, systolic murmur. In the fourth left interspace both murmurs could be heard and identified. To the right of the sternum in the second interspace there was another soft, blowing, systolic murmur. On repeated examinations no diastolic murmur was heard. Pistol-shot sounds were heard in the femoral arteries, but no to-and-fro murmur. The blood-pressure in the arms was 108 systolic and 0 diastolic, and in the legs 180 systolic and 0 diastolic.* The electrocardiogram showed normal conduction and a normal form of ventricular complexes (Fig. 2). Tracings of the radial pulse showed a very quick, collapsing pulse suggesting aortic insufficiency (Fig. 3).†

The skin of the extremities was dry and scaly. Both hands and feet showed marked loss of power. There was a bilateral foot-drop. The hands and feet were extremely sensitive to pressure, and there were patchy areas on the legs over which sensation was diminished. The calves were slightly atrophic. No edema was present over the tibiæ but there was a slight amount over the sacrum. All the tendon reflexes were absent. There was no Babinski reflex. The patient was able to take a few steps by supporting herself, and the gait when so examined seemed to be of the steppage type. The remainder of the examination was negative.

*Laboratory Findings.* The blood examination revealed: Hemoglobin, 60 per cent; red blood cells, 3,800,000; leukocytes, 8400, with 71 per cent polymorphonuclears, 24 per cent lymphocytes, 2 per cent monocytes, and 3 per cent metamyelocytes; and platelets, 300,000; the bleeding and clotting time were normal. Study of the red cells showed no basophilic stipling or abnormalities in the size and shape of the cells.

The urine examination revealed: Acid; specific gravity, 1.022; a light cloud of albumin; no sugar; no acetone; many casts, both hyaline and granular, and many leukocytes and red cells. The benzidin test for blood was positive. There was no tryosin or leucin present.

The hair was examined for arsenic, but none was found. There was no arsenic, lead or mercury in the urine. The blood culture was sterile. Cultures from the nose and throat showed nothing remarkable. The blood Wassermann reaction was repeatedly negative with cholesterin and Noguchi antigens. The spinal fluid was entirely normal in all respects, including the Wassermann and colloidal gold tests. Cystoscopic examination showed edematous ureteral openings, diminished excretion of urine, and greatly retarded excretion of indigocarmine injected intravenously. The urine was sterile.‡

* It is realized that the actual diastolic pressure did not drop to zero, but in taking the readings no fourth or fifth phase could be detected.

† Graphic cardiac studies were made and interpreted by Dr. T. M. McMillan, Philadelphia General Hospital.

‡ The basal metabolic rate was not determined. The absence of eye signs, tremor and characteristic nervous irritability, seems sufficient to eliminate the possibility of a crisis due to exophthalmic goiter.

*Treatment and Course.* On admission, a diagnosis of acute nephritis and multiple neuritis of unknown etiology was made. The nephritis appeared to be the more urgent, and treatment consisting of a low protein diet and large doses of the alkaline diuretics was instituted. After about ten days, a diagnosis of beriberi was made. The diet was then modified and autolyzed yeast given. Marked improvement followed: the urine became

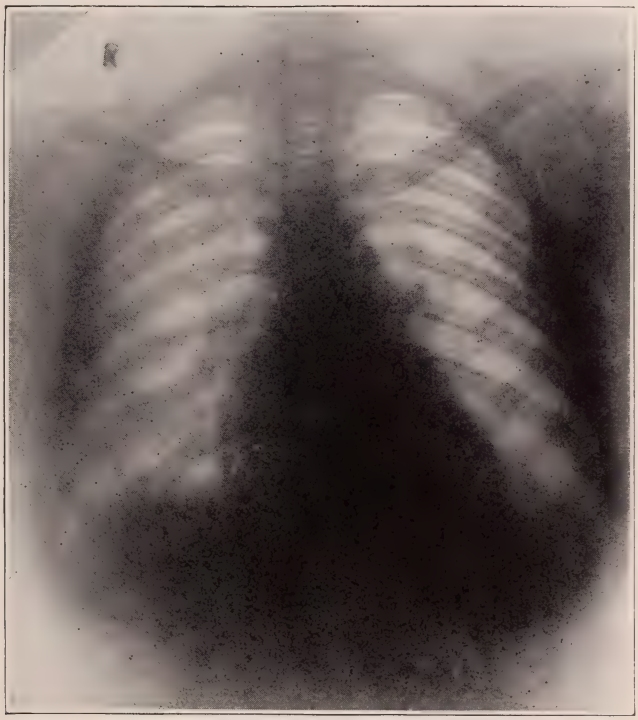

FIG. 1.—Dilatation of both sides of the heart on admission: Arch, 5.4 cm.; distance from median line to farthest right border, 5.7 cm.; distance from median line to farthest left border, 9.2 cm.; oblique, 16.3 cm.

normal; the heart murmurs gradually disappeared, the blood-pressure became normal (124 systolic and 80 diastolic); the pulsations in the peripheral arteries disappeared, and the heart became normal in size (Fig. 4). A pulse tracing taken from the radial artery was entirely normal when the patient was discharged three months after admission (Fig. 3). The peripheral neuritis gradually subsided, and at present the patient is able to walk and is at home doing her own housework.

Comment. The diagnosis of beriberi in this patient seems justified because of (1) the history of a prolonged high carbohydrate

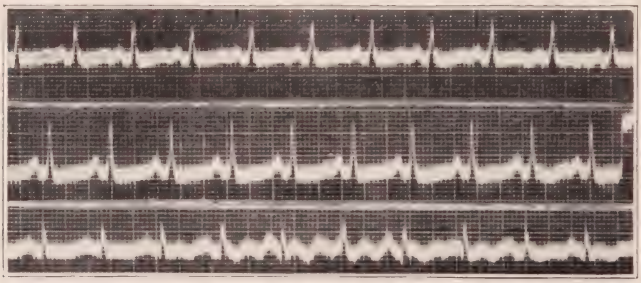

Fig. 2.—Normal conduction time and normal ventricular complexes at time patient was admitted.

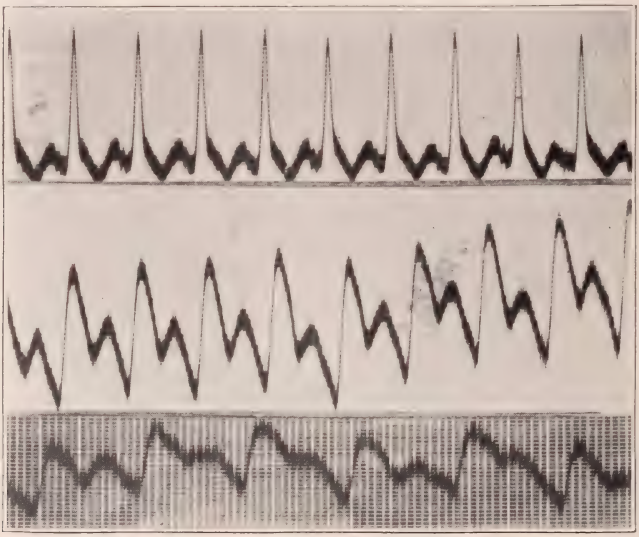

Fig. 3.—Pulse tracings from the radial artery: The top tracing shows the collapsing pulse suggesting aortic insufficiency; beginning of upstroke to peak of primary wave, from 0.06 to 0.065 second; beginning of upstroke to predicrotic summit, 0.12 second, against 0.23 second in normal persons; this tracing should be compared with the middle tracing, which was made when the patient was discharged; the bottom tracing was made at the same time as the middle, but at twice the rate of speed, in order to bring out the time relationships more clearly; both are entirely normal.

diet deficient in vitamines; (2) the clinical picture of peripheral neuritis with myocardial failure—the ordinary causes for these

conditions having been eliminated, and (3) the rapid response which the patient made to specific therapy.

The nephritis is difficult to explain. Beriberi ordinarily does not produce a nephritis. Whether it occurred as an independent condition or as the result of intravenous medication, it is impossible to say. The possibility of some toxic substance in the starch itself,

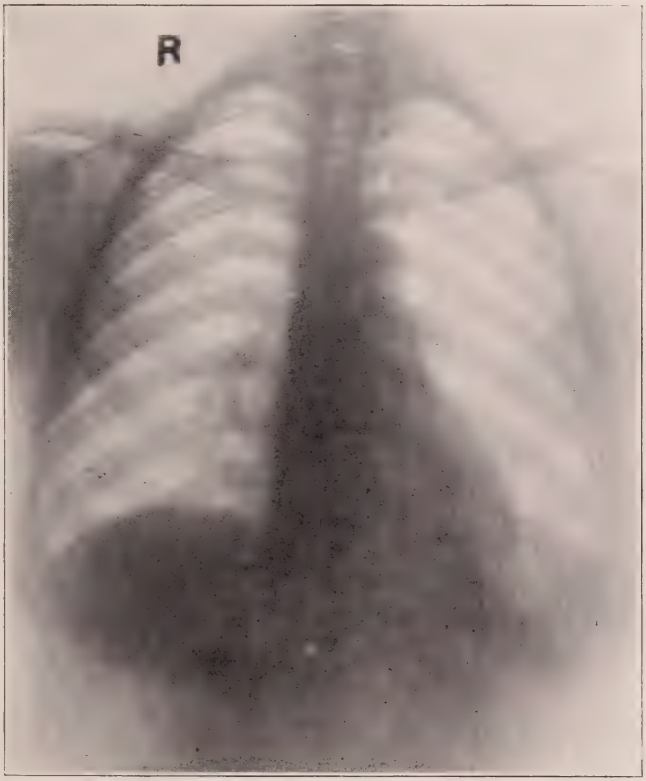


FIG. 4.—Condition when the patient was discharged: Arch, 5.4 cm.; distance from median line to farthest right border, 3.9 cm.; distance from median line to farthest left border, 8.2 cm.; oblique, 14 cm.

which could produce both a nephritis and a peripheral neuritis, was carefully considered. However, the analysis of gloss starch given in the textbooks, as well as that submitted by the manufacturer of the particular starch in question, makes this possibility very unlikely.

The peculiar cardiac findings simulating aortic-valve disease

afford material for much interesting speculation. Vedder has shown that beriberi is a disease of the entire nervous system, and it seems possible that a paralysis of the vasomotor system, in which the heart was pumping blood into relaxed and dilated arterioles, could give the vascular signs presented by the patient. On the other hand, a relative aortic insufficiency might have occurred as a result of the dilatation of the heart, although if this were true it seems as though a diastolic murmur should have been present.

RESULTS OF CHEMICAL EXAMINATION OF THE BLOOD.

| | October 20. | October 27. | November 26. |
|---|---|---|---|
| Urea nitrogen | 20.0 | 45.0 | 11.0 |
| Uric acid | 6.6 | 8.0 | 4.0 |
| Sugar | 155.0 | 180.0 | 110.0 |
| Creatinin | ..... | 1.4 | |
| Carbon dioxide per 100 cc | ..... | 43 cc | |

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## OCTOBER 26

## PELLAGRA AND PELLAGROID AT THE PHILADELPHIA GENERAL HOSPITAL

BY JOSEPH V. KLAUDER, M.D.

*(Abstract)*

THE presentation is based upon an analysis of 42 cases of pellagra at the Philadelphia General Hospital: 22 cases were personally observed during the past two summers, the remaining number comprised recorded case histories. This number does not represent the incidence of pellagra at the Philadelphia General Hospital, since all the cases of pellagra during the past two summers were not observed by the essayist. Moreover, all records of pellagra patients are not readily accessible from the files in the record room. The study is still in progress.

Of the 42 cases, 29 were men and 13 were women, the age of the majority ranged from forty to sixty years, excepting a few patients

in the early thirties. In only 1 instance was there a history of recent residence in southern states where pellagra is endemic. Different races were represented; there was, however, only 1 Negro. None of the patients were Jews. Some writers point out that pellagra in endemic areas is rarely seen in the Jew.

A history of chronic alcoholism was very conspicuous in all but a few of the cases; likewise, the history of an insufficient or unbalanced diet.

The cases were classified into three main groups. Group I included true endemic or conventional form of pellagra. Group II included the acute form, frequently fatal, the initial symptoms of which suddenly appeared following an alcoholic debauch. Group III, the dermal form, characterized by cutaneous lesions with none or few of the other symptoms of pellagra. This form was seen only in patients recovering from a prolonged alcoholic debauch, excepting in 1 patient with pulmonary tuberculosis and another patient with inoperable gastric carcinoma.

Lantern slides of the cutaneous lesions on the patients in the three aforementioned groups were shown. The clinical features of the cutaneous picture of pellagra, atypical lesions and differential diagnosis were discussed. A brief narration of the history and a discussion of the conspicuous symptoms presented by the patient whose photograph was shown was given.

The history of all the patients in Group I, were typical of pellagra relative to the gradual loss of strength, headache, dizziness, insomnia, various pains, depression, gastric symptoms, notably sensation of burning in the stomach and mouth, recurring attacks of an eruption on the exposed parts of the body. In the majority of these patients the duration of symptoms was less than two years, in one it was five years and in another twenty years (this patient is at present in the hospital). Of the 17 patients in this group all were chronic alcoholics excepting 4. In most all there was definite history of dietary insufficiency; for example, a young woman (no history of alcoholism) in order to lose weight partook of a self-prescribed diet in which all animal foods, excepting cheese and also milk, cooked, in her food were eliminated. A year following such diet she lost 40 pounds in weight and complained of weakness and depression. A short time later a dermatitis of the exposed parts appeared, with diarrhea and stomatitis. In another patient the diet consisted for a long period of wine and spaghetti.

All patients in Group I succumbed excepting 3, 2 of whom are still in the hospital (the prognosis is grave). The terminal picture was one of extreme prostration, dermatitis of a pellagra character on the exposed parts or pigmentary remains of the eruption with a dry, wrinkled skin, stomatitis of variable degree, persistent diarrhea recalcitrant to treatment, frequently pupillary abnormalities, with increased patella reflexes, a delirium accompanied by low mutterings, coarse muscular twitchings of the face and hands, picking at the bedclothes or irregular jerking movements of the extremities. In some the temperature was elevated and irregular. This picture recalls that of a patient in the third week of severe typhoid and also resembles a condition sometimes seen in delirium tremens. This syndrome has been described as typhoid pellagra.

The mental disturbances in pellagra were discussed. Psychiatrists point out that there is no characteristic mental picture of pellagra; if one is to be formulated it would approach that of the acute psychosis of alcoholism. Mental disturbances seen in the series were paranoid states, acute psychosis, usualy sudden in onset with complete disorientation and marked increase of psychomotor activity, visual and auditory hallucinations, marked depression with suicidal tendency.

Thirteen patients comprised Group II: In all the initial symptoms of pellagra appeared following a prolonged alcoholic debauch in which there was a definite history of dietary insufficiency, indeed, no food at all or very irregularly for some time. In these cases the cardinal symptoms were dermatitis of the involved parts, stomatitis, diarrhea and frequently an acute psychosis. Some patients eventuated into the aforementioned typhoid state and succumbed. The mortality in this group was about 50 per cent.

Group III, comprised patients who presented a sharply marginated dermatitis, mahogany-brown in color, of the hands, in some the face and hands, appearing after an alcoholic debauch. The dermatitis was confined to the dorsum of the hands or to varying portions of the forearm or the entire forearm. There were few or no other symptoms of pellagra; in some a mild stomatitis or a beef-red tongue or a mild diarrhea. From the history these were the intitial symptoms, excepting in one patient a similar gloved dermatitis appeared on several occasions following an alcoholic debauch. A pellagra history, otherwise, could not be obtained from this patient.

From the reports of others, alcoholism has at times been regarded as an important predisposing factor. Alcoholism among pellagra patients was mentioned in Casel's original report on pellagra, published in 1762.

The relation between the dermal form (Group III) and true endemic form of pellagra (Group I) was discussed. In this regard Goldberger was quoted to the effect that the varying dominance of one or the other symptom or symptoms is in all probability intimately related to as yet obscure variations in some dietary factor or factors. Goldberger recently suggested that pellagra may include at least two etiologically distinct though closely related syndromes: (1) The pellagra with eruption but with slight other symptoms, which Goldberger calls the dermal form, and (2) the pellagra with subjective and other manifestations but no eruption, the *pellagra sine pellagra*.

The relation between sunlight and the eruption of pellagra was discussed. Studies were made to determine photosensitivity of the skin of pellagra patients by means of the Alpine lamp. No photosensitivity could be demonstrated. Studies were also made in the direction of demonstrating a lytic substance in the blood of pellagra patients that is activated by the actinic ray. The basis of such studies was the fact that pellagra is regarded as a photosensitive disease. In such diseases hematoporphyrin apparently plays some rôle. Furthermore, the theory of Jobling and Arnold is to the effect that the circulation in the blood of porphyrins or other photosensitive substances is responsible for the skin manifestations of pellagra. These studies, which were detailed, were negative. Other studies, however, are in progress.

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## The Effects and Disappearance of Orally Administered Hydrochloric Acid in Normals and in Cases of Anacidity

BY EDWARD ROSE, M.D.
(By Invitation.)

The adequacy of the customary 1-cc dose of dilute hydrochloric acid given to patients with gastric anacidity has oftened been questioned. Observations by Leo, by Crohn and by Shaw and others have shown that 2 cc or more of dilute hydrochloric acid had to be given before free acid could be found in the stomach after a test-

meal, while doses up to 12 cc at times failed to give this result. Two years ago Vanderhoof presented a clinical study of 7 cases of combined sclerosis with achlorhydria, but without anemia, and reported marked improvement after the administration of 4 to 8 cc of dilute hydrochloric acid with meals over a period of years.

The work which forms the basis of this communication was done in the wards of the Medical Division of the University of Pennsylvania Hospital and in the laboratory of the Department of Research Medicine, in collaboration with Dr. Richard A. Kern and under the supervision of Dr. J. H. Austin. We have been controlling our use of hydrochloric acid therapy in various conditions by studying the effects of various doses of hydrochloric acid upon the gastric contents of individuals with and without acidity and wish to present briefly our observations. In addition to total and free-acid determinations, observations were made on the pH, on pepsin content and, because of the possible factor of duodenal regurgitation, on trypsin content as well. Studies are now in progress on the concentration of chlorides and total base in the gastric content under various conditions.

After a preliminary study on the effects of acid in normal individuals, the results of which are in accord with those of previous observers, we studied the effects of acid administration fifteen times in 10 cases of anacidity—8 of them primary pernicious anemia, 1 gastric syphilis and 1 idiopathic anacidity. Dilute hydrochloric acid, U. S. P. strength, was given with the usual Ewald test breakfast in various doses ranging from 1 to 14 cc. It is generally accepted that the highest concentration in which hydrochloric acid occurs free in the gastric juice is about 125 to 126 millimolar. This concentration corresponds to 14 cc of U. S. P. dilute hydrochloric acid in 360 cc of the water of the test-meal and we did not exceed this concentration. Analysis was made of the fasting contents and of specimens removed after the meal by the fractional method. Free and total acid were determined in the usual way; pH determinations were made by colorimetric comparison on a porcelain plate with equal amounts of standard solutions of a known pH and a series of indicators; peptic and tryptic activity were determined by Itakura's modification of the Fuld-Gross method.

We realize that figures obtained by the fractional method of gastric analysis are not representative of a uniform composition of the stomach content at any one time, but we believe that the variations observed are of some value.

(Lantern slides are here exhibited on the screen.)

The first slide shows the type of free-acid curve obtained by Crohn and by Shaw after acid administration in anacidity. The numbers represent the total cubic centimeters of acid given, and it will be observed that the highest acid titers obtained were when a large amount of acid was given in divided doses at intervals after the meal, at the times indicated by the crosses.

The second slide shows in brief our findings with regard to the appearance of free acid after acid administration to patients with anacidity. In addition to the 2 cases here noted, we have repeatedly found in other instances that a 1-cc dose of acid failed to be followed by free hydrochloric acid. The larger the dose of acid given the more frequently did acid appear and the greater its titer.

The third slide shows the free-acid curves in the five instances where free acid was found out of 9 cases given 4- to 8-cc doses. The acid was given in a millimolar concentration of 120 in 2 of 9 studies, and in both instances was followed by free acid, as shown by the solid line curves. When given in less than 120 millimolar concentration free acid was found in only 3 of 7 instances, as shown by the broken line curves. It will be noted that the free acid rose higher when the more concentrated acid had been given. The highest concentration of free hydrochloric acid is seen usually in the first specimen removed after the test-meal, and rapidly falls thereafter.

We gave acid in 13- to 14-cc doses and in millimolar concentration of 120 four times to 3 patients and even with this large dosage obtained free acid in the gastric contents only three out of the four times. The curves of the free acid are shown in the fourth slide. The curves are similar in type to those obtained after 4 to 8 cc of acid.

We had considerable difficulty in getting patients to take 14 cc of acid. We tried it ourselves and found it a most unpleasant dose and from a clinical standpoint wholly impracticable: 4 to 8 cc doses, however, are easily taken—more easily in weak tea or buttermilk than as given in these experiments.

In addition to acid dosage, an important factor in determining the extent to which one can produce and maintain an increased gastric acidity has been, in our cases, the underlying clinical condition. The presence of free acid was rather easily secured in both our patients without anemia and in the pernicious anemia cases

while in a remission, while even the largest dose of acid once failed in a patient with primary anemia at a time when the anemia was very severe.

We have studied the pH of the gastric content under the conditions of these experiments. In the presence of so-called free hydrochloric acid the pH is 3 or lower and varies with the degree of free acid present. In the absence of free hydrochloric acid there may be a variation of pH from at least 3 to 7 or above. Within this range the ordinary determinations of total gastric acidity give no information as to the pH. It is noteworthy that in a small group of apparently normal individuals there is a persistent achlorhydria without any symptoms of gastric malfunction. It is conceivable that in these persons, in spite of the absence of free hydrochloric acid, the pH of their gastric contents might still be low enough for effective though not optimal peptic action. We actually found this to be the case in a patient with syphilis of the stomach whose gastric contents showed no free acid at any time. The pH range in this patient was between 3.5 and 3.9. Observations concerning the pH in the absence of free hydrochloric acid have been reported by Babbott, Johnston and Haskins. It has long been known that in milk-fed infants there is usually no free acid in the gastric contents in the first year or so of life, yet there is good peptic activity. Babbott, Johnston and Haskins found that in such infants the pH ranged between 3.5 and 5.

It seemed possible, therefore, that small doses of acid insufficient to produce free hydrochloric acid might still sufficiently alter the pH of the gastric contents as to materially influence gastric function and thus explain the good clinical results reported following small acid dosage (1 cc).

We found, however, that 1 cc of acid not only failed to produce free hydrochloric acid, but also did not appreciably lower the pH in any of our cases. There was, however, in 2 of the 4 instances where doses of 4 to 8 cc of acid failed to produce free HCl, a definite shift in pH from the neighborhood of neutrality to 4.2 and 3.8 respectively, as shown in the fifth slide.

It is, of course, well known that electrometric and colorimetric determinations of the pH of various body fluids may not give the same results, the variation being due largely to protein content. Stokes and Kahn, in work recently reported before the Physiological Society, found in solutions (gastric content) with a pH above 3

occasional variations of from 1 to 1.5 pH; a few times, in solution with a pH of 4 or 5 (electrometrically determined), the difference was as great as 2. Our determinations were made by a modification of the colorimetric method, were not checked electrometrically and hence may or may not represent the true pH of the gastric content—variations following acid administration do not, however, lose their significance because of this fact.

As regards available pepsin, which in all of our patients was less than in normals, in no instance did the administration of acid in doses large or small increase it significantly. In this connection we wish to refer to 2 patients who have been under observation for two years and one year respectively. Both have pernicious anemia and 1 of them (the two-year case) has cord changes. Both patients are in a state of remission with steady improvement and have been receiving acid in 2- to 5-cc doses off and on since they first came under observation. Yet even after this prolonged acid therapy in neither instance has there occurred any increase in the available pepsin, which was considerably below normal. Neither has there been spontaneous appearance of free hydrochloric acid or any significant change in the free-acid curves that follow the administration of acid.

Trypsin has been found constantly present in the fasting contents of these anacidity patients, which suggests that regurgitation of alkaline duodenal contents is a regular phenomenon in anacidity and probably a factor in the neutralization of the administered acid. The importance of swallowed mucus and saliva in neutralizing gastric acidity should not be overlooked. Working with gastrostomized children, Kahn and Stokes have found that gastric content removed through the gastrostomy opening had at times about twice the acidity of chyme removed almost simultaneously through a stomach tube immediately after it had been passed. Certain of our achlorhydric patients showed a decidedly greater degree of acidity when dilute hydrochloric acid was introduced through a stomach tube than when the same dose was swallowed and free HCl was found present for a longer period. We suspect that neutralization by swallowed saliva and mucus was the cause.

Summary. 1. The usual clinical dose of hydrochloric acid (1 cc) in achlorhydria not only fails to produce free hydrochloric acid in the gastric contents, but also does not materially lower the pH from the range near neutrality.

2. Four- to 8-cc doses of acid may fail to change the acidity, but more often there results a fall in pH to less than 4, a change sufficient to influence peptic activity even though not enough to give a positive reaction for so-called free hydrochloric acid. The pH may be lowered to less than 3 with the appearance of free acid. After maximal doses free acid has been found for as long as fifty minutes. The changes in gastric acidity depend upon the amount of acid given, upon its concentration and upon the type and severity of the underlying clinical condition. A 4- to 8-cc dose of acid is usually adequate and is the highest dose that we find clinically practicable.

3. Acid administration, even when continued over a long period of time and in large doses, has not in our cases increased the available pepsin or caused the spontaneous appearance of free acid in the stomach.

4. These observations suggest that if the purpose of acid therapy in pernicious anemia is to alter the acidity of the gastric contents doses of at least 4 to 8 cc. of dilute U.S.P. hydrochloric acid should be given with each meal.

## The Diagnosis of Abdominal Tumors

BY JOSEPH SAILER, M.D.

Among the most difficult of conditions to diagnose, I have always found that tumors of the abdomen take the first place. This must be understood as a general statement. Some tumors declare themselves at once; others are diagnosed perhaps at the operation or autopsy; sometimes only in the laboratory.

The diagnosis is to be made, as in the majority of all cases, by the correlation of information obtained from the history, physical examination, course and laboratory findings, *x*-ray studies; and particularly by the findings at operation, histological diagnosis, and chemical and bacteriological examinations.

The important features of the history are the mode of onset, the occurrence and nature of pain, the effect upon the general health and various special associated symptoms.

The physical examination is more valuable if made systematically, and I have employed such a systematic examination with satisfaction for a long time. It is as follows:

1. Location.
2. Size.
3. Shape.
4. Surface.
5. Consistency.
6. Motility.
7. Percussion.
8. Auscultatory findings.
9. Special palpatory findings; friction; crepitation.
10. Changes in the tumor environment, including evidence of obstruction and pressure.
11. Changes in the general condition of the patient.

1. The location can be described in various ways. The tumor or tumors may be in the wall or cavity of the abdomen; within, or a part of, an organ. The usual division of the anterior surface of the abdomen into nine regions is most convenient. For the back the bony landmarks suffice, and the sides require no subdivision.

Tumors of the wall include the various skin-growths, lipomas and fibromas, hernias, abscesses, intramuscular hemorrhages, metastatic growths, an undescended testicle. Many of these are easily diagnosed; many are not peculiar to the abdominal wall; but others, such as the intramuscular hemorrhage or abscess that occurs in the recti muscles in pneumonia, and metastatic malignant tumors, are difficult to diagnose.

Tumors of the abdominal cavity are so numerous that they require special classifications. This will be given later. The tumors that are of an organ include all the masses caused by enlargement of the entire organ, or of part of the organ, or morbid conditions invading the organ, either from some source in the organ or from the outside; parasitic growths; infectious granulomata; inflammatory growths; malignant tumors; cysts; calcareous deposits; foreign bodies; hypertrophies and distentions. Tumors lying outside the organs are less numerous. They include the tumors springing from the walls of the abdominal cavity, particularly various forms of sarcoma and endothelioma, including osteomas; vascular tumors, including the aneurysms; foreign bodies.

2. The size of the tumor varies greatly. The largest tumors are some of the cystic tumors of the ovary, their weight often exceeding the weight of the patient: One of my cases weighed 147 pounds before the operation and 70 pounds afterward. Next in size are

the enlargements of the liver, spleen and uterus; perirenal abscess, malignant tumors, especially linitis plastica, retroperitoneal sarcomata, gelatinous or colloid carcinoma of the colon, and osteosarcomata, endotheliomata, desmoids, and rarely an infectious granuloma, as actinomycosis. Multiple small but palpable tumors of the abdominal cavity are usually lymph glands, especially a chronic tubercular form. A fibroma of the pro- and subperitoneal tissues, resurrected by Witney and Harrington and copied by Pagenstecher, was enormous.

3. The shape may be *globular*, as some of the uterine fibromas, fibromas of the mesentery and the osteosarcomas; *flat*, as the tubercular growths of the great omentum; *nodular*, as fibromas, secondary carcinomas, masses of lymph glands.

4. The surface may be *smooth*, as in diffuse enlargement of the liver, spleen, uterus, kidneys and in tumors springing from the periosteum; *rough*, as in certain forms of cirrhosis of the liver, carcinoma of the peritoneum, usually perceptible after the ascitic fluid has been removed, in hydatid cysts occasionally, and in some of the carcinomas of the stomach; *nodular*, as in metastatic growths in the liver, in tuberculosis of the lymph glands, especially the retroperitoneal, in Hodgkin's disease, in subserous fibromata of the uterus. The nodules vary greatly in size in different tumors; sometimes in the same tumor. Indeterminate surface—I know no better word—is found in the colloid carcinoma of the colon.

5. The consistency can only be compared to known tissues. Bony consistency only occurs in bony tumors, exostoses, osteosarcoma and osteomyelitis of the pelvic bones. A firmness similar to that of a cirrhotic liver occurs in fibromas; in various enlargements of the liver; cirrhosis; passive congestion; carcinoma; in enlargements of the spleen, as in Banti's and Gaucher's disease; in leukemia, in chronic malaria and syphilis of the spleen, and in a form of chronic tuberculosis of the spleen; in some fibromas of the uterus, in hypernephromas and polycystic kidney; in some carcinomas and sarcomas; in retroperitoneal sarcomas; and in massive actinomycosis, of which I have seen one case. A consistency about that of a relaxed muscle is observed in acute splenic tumor; in some acute inflammatory enlargements of the liver; in degenerating fibromas. Soft tumors are usually gelatinous in form; sometimes a distended cecum or descending colon will feel soft, but a fecal impaction may vary from dense hardness to a peculiar soft, claylike consistency, that

is almost characteristic. Fecal masses are often felt as tumors to the gastric side of an intestinal obstruction, and vary greatly in consistency, and it is characteristic that they may vary in density at different times.

Fluctuating tumors are of many kinds, free fluid as in ascites, circumscribed fluid, in all forms of large cysts that are accessible, particularly those of the uterine adnexa and the pancreas, hollow organs filled with fluid, as the gall-bladder, the urinary bladder, the renal pelvis, rarely detected, the stomach and the cecum. The detection of flucuation is often difficult. If the tumor is superficial, gentle direct percussion with the receiving hand flat upon the tumor mass is most effective; if deep, bimanual palpation will sometimes succeed. Tumors containing gas produce two forms of sensation—a tense, elastic consistency resembling that of a rubber balloon, often felt in the distended stomach and in the general elastic distention of tympanites; and I once felt it in a distended Meckel's diverticulum as a small localized tumor. Large, localized gas tumors, following perforation, usually occur in the right hypochondrium and cause disappearance of the liver dulness. In intestinal obstruction Nothnagel describes distention of the intestines and colon very fully. Localized distention of the intestine occurs occasionally above intestinal obstruction. The most extreme form of the elastic gas tumor is the phantom tumor that is observed in certain hysterical women. Soft gas tumors, if they may be so called, occur in the stomach, usually accompanied by splash or gurgling, if bimanual palpation is used, and in the colon. Finally, foreign bodies have the consistency peculiar to themselves, as hemostatic forceps, a gauze pad, a stomach stuffed with grass and straw, to mention those only within my own experience, undiagnosed during life, except the hemostatic forceps which were discovered by a colleague.

6. Percussion is of value. A few tumors are tympanitic: the acutely distended stomach, the distended colon. The Meckel's diverticulum that I observed in a case of typhoid fever was resonant throughout its course until removed by operation. Indeed, it seems as if a small tympanitic tumor in the umbilical region that persists, although the bowels move freely and there is no evidence of interstitial obstruction, can be nothing else. Occasionally solid tumors will yield a muffled tympanitic note in certain parts. Apparently this occurs only in tumors growing from the serous coats of the intestines, leaving these intestines as distended tubes within their substance. I have discovered no description of this sign,

although the tunneled tumor is well known, but I have observed it in two abdominal tumors, both in the left upper quadrant. One of these tumors was an endothelioma, and the other a remarkable case of actinomycosis, the nature of which was unsuspected and only discovered by the histological examination. Some tumors of the upper abdomen, chiefly infiltrating growths of the great omentum, may also yield a dull tympanitic note. Percussion may also aid in determining the boundaries of tumors, and particularly the presence of respiratory or passive motility.

7. Tumors may have a variety of forms of movement. These may be classified as follows: (*a*) Respiratory; (*b*) passive; (*c*) gravity; (*d*) spontaneous; (*e*) pulsation, subdivided into intrinsic and transmitted; (*f*) passive deformation, subdivided into elastic and plastic.

(*a*) Respiratory motion is transmitted by the movement of the diaphragm. Naturally tumors of the upper part of the abdomen are the most susceptible to this movement. These are tumors of the liver, spleen, kidneys and stomach. There is some question regarding the movement of the pancreas. The pancreas is a movable organ. Dr. John B. Deaver has assured me that in the abdominal cavity it can be freely pushed about. Pawlow's pancreatic fistula requires mobility of the dog's pancreas, and the question can easily be tested at any autopsy. On the other hand, in pancreatitis, the organ is often fixed or partially fixed by adhesions, and if there is a palpable carcinoma of the head of the pancreas it does not usually exhibit respiratory movement. In cases of chronic pancreatitis there is sometimes a point of tenderness about 2 cm. above the umbilicus. If, while pressure is made upon this point, the patient takes a deep inspiration, the tenderness disappears. I have attempted to explain this by supposing that the head of the pancreas moves downward from under the pressing finger. If this explanation is correct, it involves a respiratory movement of the pancreas.

Respiratory movement is, as a rule, easily detected. In the case of the liver, using bimanual palpation, with firm pressure, a diffusely enlarged liver will separate the palpating hands during inspiration; a hard liver with a sharp edge will impinge upon the upper hand and the edge will suddenly slip under it, giving a characteristic sensation. If there are nodules, they can be felt to move under the upper hand. An enlarged and palpable gall-bladder moves with the liver and may be felt sometimes distinctly below the liver's

edge. The spleen, if sufficiently enlarged to be felt beneath the costal margin during deep inspiration, can always be felt to move freely. In a case of eventration of the diaphragm, a large spleen, due to typhoid fever, could not be felt because it was high in the thoracic cavity. Even the huge spleen of leukemias, the splenic anemias and chronic infectious diseases move freely. Tumors of the kidneys and inflammatory enlargements, as the congenital multiple cystic kidneys, may, as a result of their size, be dislocated downward and no respiratory movement may be perceptible, but the ptosed kidney is easily felt to move downward during inspiration, and to return upward with a sudden slip during expiration.

Tumors of the stomach, especially tumors of the pylorus, if not adherent, and sometimes if they are adherent to the gall-bladder, move with respiration, but they may change their position and sometimes cease to be palpable, depending apparently upon the condition of the stomach; that is, if it is contracted, they may lie above the costal border, to reappear when the stomach is more distended or if the patient stands up. Tumors of the great omentum, of the transverse colon and small intestines may exhibit respiratory motility. This is, in these cases, less important than the other signs by which they are recognized.

Tumors of the upper part of the abdomen that do not move with respiration are the enlarged retroperitoneal lymph glands, abdominal aneurysms, abscesses and all tumors of the abdominal wall. Paralysis of the diaphragm would prevent respiratory movement. I have seen an instance, confirmed by *x*-ray, in a case of multiple neuritis, and the movement of the abdominal organs could not be observed. Eventration of the diaphragm draws the upper abdominal organs upward and therefore they are not palpable; nevertheless, the diaphragm moves slightly, and an enlarged organ presenting beneath the costal border might be felt to move. Movement may also be detected by percussion. In slight enlargement of the spleen and liver, if the pleximiter finger is placed parallel to the costal margin and continuous percussion made during deep respiration, if the liver or spleen are enlarged, the note will become duller at the end of inspiration, and this is a trustworthy sign.

Respiratory movement is obscured or masked if there is great tympanites or ascites, or crowding upward of the diaphragm as by a neglected ovarian cyst or a pregnant uterus, in massive edema of the walls of the abdomen, such as occurs in cardiac decompensation;

in peritonitis with rigid abdominal walls and if there is excessive tenderness preventing palpation.

(*b*) Passive motility means that the tumor yields to external force. This applies to all tumors, excepting those attached to the skeleton and to the walls, or in the walls of the abdomen. Even the latter may move as much as the walls themselves, and in the case of relaxed abdominal walls this is considerable. The degree of motility varies. It is greatest in the case of tumors of the transverse colon, in the so-called floating kidney and the rare dislocated spleen, and in some pedunculated fibroids of the uterus. It is less, but easily perceived in the enlarged organs, and in glandular tumors of the mesentery. Osler describes an abdominal aneurysm, saccular in type, that could be pushed from side to side. Passive mobility does not occur in tumors of the retroperitoneal glands, in sarcomas springing from bones, in abscesses, unless they are attached to or within organs. Sometimes it is possible to determine that a tumor is part of, or attached to, an organ by the fact that they both can be moved passively together. I recall a case of a tumor of the lower abdomen, associated with the Epstein-Pel type of fever and leukocytosis, which had persisted for six months. By vaginal examination it was found that the tumor moved with the uterus, and at the operation a suppurating dermoid cyst was found attached to the uterus. This fact is also helpful in determining that a tumor beneath the liver is an enlarged gall-bladder, and in a huge multilocular tumor of the left side of the abdomen now under observation, simultaneous movement of the nodules during manipulation proves that they belong to one mass or organ, presumably the spleen. Gall-bladder tumors move with the liver, and if the liver is lifted the tumor moves with it. Passive movement may also be observed after the inflation of the hollow organs, usually the stomach, to which they are attached.

(*c*) Gravity movement, that is a change of the position of the tumor to the most dependent part if the patient shifts his position, is rarely pronounced. In a slight form it is very common. Tumors of the pylorus may be more easily palpated at times if the patient is erect, and the shift under these conditions is of some diagnostic significance. The most remarkable case of this kind that I have observed was a carcinoma situated in the center of a festooned transverse colon. This tumor would gravitate to one flank if the patient, a woman, laid upon that side, and then, when she rolled

on the other side would, in the course of fifteen minutes, be found in the other flank. Cysts in the lower abdomen, if not too large, may also respond moderately to gravity. The fixed tumors do not respond and those in the upper part of the abdomen may even seem to move upward, often causing a pyloric tumor to disappear, when the patient is erect, as a result of a change in relation to the other organs. As a rule, however, tumors or enlargements of the liver, kidneys, spleen and stomach are more easily felt if the patient is examined in the erect posture.

(*d*) Spontaneous movement occurs in tumors of the gastrointestinal tract and in the pregnant uterus. Tumors of the pylorus may be seen and felt to move as a result of peristaltic contraction. A hypertrophic pylorus may be felt to harden and relax rhythmically. In the only case of this nature that I have observed I noticed that the hardening occurred at intervals of nineteen seconds, or occasionally thirty-eight seconds, in accord with Cannon's statement. Visible peristalsis of the stomach is usually present in pyloric obstruction. There are two types of spontaneous movement of the stomach, a sudden stiffening of the whole organ persisting for several seconds; and the moving peristaltic wave. If the tumor causes a partial intestinal obstruction, especially if near the ileocecal valve, there will be a more or less vigorous peristalsis in the proximal portion of the intestinal tube; sometimes producing a hill and valley abdomen in constant motion. A comparison to the stormy ocean is, to my mind, more appropriate. If not adherent to surrounding structures, the tumor may be felt to move slightly with the peristaltic wave. This was noted in the tumor of the transverse colon to which reference has been made. Spontaneous movement occurs in tumors of the ascending and descending colons, and they can sometimes be moved passively, especially tumors of the ascending colon. Transmission of spontaneous movement is probably rare, at least I have never observed it occurring to a tumor overlying the gastrointestinal tract. The absence of spontaneous movement does not exclude a tumor of the stomach or intestines, but its presence is of importance and is almost pathognomonic. It is unnecessary to do more than mention the spontaneous movements of the pregnant uterus. Spontaneous movement occurs rather violently during the appearance of phantom tumors.

(*e*) Intrinsic pulsation occurs in aneurysms, in the liver during tricuspid disease, in the spleen during aortic regurgitation, in pul-

sating empyema necessitatis and in a few sarcomas. Osler makes a point of the fact that aortic aneurysms have expansile pulsation, and that the normal aorta does not. However, a sclerotic aorta in an emaciated old person may be felt to expand with each pulsation, and the difference is one of degree rather than of kind. The size of the pulsating mass, the *x*-ray and a positive Wassermann reaction are of more importance than the detection of thrill and bruit, which are rarely present in aneurysms of the abdominal aorta. Sibson's sign, a palpable diastolic shock over the aortic cartilage, is usually present, but is only confirmatory or suggestive and not decisive. The location of the abdominal aneurysms depends upon the artery involved. Pulsation of the liver occurs in tricuspid regurgitation, and is said to occur in tricuspid stenosis. It is also said that the differential diagnosis can be made by noting, in a simultaneous tracing of the liver and of the apex beat or jugular vein, whether the liver-pulse precedes the apex beat or is synchronous with it, that is, one-twentieth of a second behind it, or whether it is synchronous with the *A* or with the *C* wave of the jugular pulse; the assumption being that in tricuspid stenosis the liver-pulse is the result of the vigorous contraction of the auricle, and in tricuspid regurgitation to the contraction of the ventricle. I have made many of these tracings, but have never yet obtained a tracing that could be interpreted as caused by stenosis; but as stenosis of the tricuspid valve was not found in the cases that came to autopsy, I am not in a position to doubt the statement that the differential diagnosis can be made. Pulsation of the liver may be detected by placing the edge of the hand beneath the edge of the liver, by bimanual palpation, or by placing the hand flat against the back just below the twelfth rib. The latter is most certain, for only the liver can give rise to pulsation in this region. A pulsating liver is suspected if there is jugular pulsation and the physical signs of mitral or tricuspid cardiac disease are present. The liver is enlarged but usually shrinks if the tricuspid valve becomes competent.

Pulsation of the spleen in aortic disease was first noted by Gerhardt. It is rare, but occasionally, if the finger is placed parallel to and just below the tenth rib, the edge of the spleen can be felt pulsating against it. I have observed this only twice and in neither case was I able to satisfy myself that it was an intrinsic and not a transmitted pulsation. Neither case, unfortunately, was in a hospital, otherwise it might have been possible to observe the spleen

with a fluoroscope and possibly to settle the question. It was not even possible to determine whether the spleen was enlarged or only pushed downward.

Pulsating empyema necessitatis is rare, although a number of cases have been reported. It may appear in any point along the costal border. The tumor is usually large, pulsates vigorously, the pulsation is expansile and the diagnosis is confirmed by aspiration. It has been mistaken for an aneurysm, but as a rule the location excludes this diagnosis. Henry has reported multiple tumors of this type.

Pulsating tumors, usually sarcomas, are rare. I saw such a tumor in the stump of an amputated arm; the pulsation was expansile and so vigorous that it shook the whole body. I have seen none in the abdomen.

Transmitted pulsation occurs in solid tumors overlying the abdominal aorta. It is not expansile, but the force of the pulsation is increased by pressure. I have observed it several times in tumors of the pylorus. Less frequently pulsation is transmitted from the iliac arteries.

(*f*) Change in shape, produced by pressure, occurs in two forms. Either the tumor resumes its original shape as soon as the pressure is released, or it remains permanently altered. Elastic deformation is usually readily recognized in all cystic and gaseous tumors. It is most valuable as a physical sign in the case of the distended gall-bladder, but it is also useful to recognize it in other cysts. In gaseous tumors it is of very little importance. Plastic deformity is limited to fecal masses. It does not occur in all forms, because the fecal mass may be too firm to be indented, unless an undue amount of pressure is used. It is, however, pathognomonic, and is therefore of great value. Fecal tumors are not always recognized as such. In one such mass, occurring in a large diverticulum of the sigmoid, the roentgenologist, the surgeon and the internist all agreed that it was a solid tumor of the pelvis, and only an operation revealed its true nature.

8. Auscultation is of relatively little importance, and none of the signs are of great significance for the diagnosis of abdominal tumors; nevertheless there are various sounds that may be confirmatory or aid in determining the location of the growth. In the stomach a persistent splash suggests pyloric obstruction. It is most easily heard by placing the bell of the stethoscope just below the xyphoid

cartilage to the left of the median line. Succussion is then made just to the left of the umbilicus. A splash may be heard in a distended or relaxed colon. Occasionally squirting sounds may be heard in the region of partial intestinal obstruction. As similar sounds are not uncommon when no obstruction exists, they are by no means pathognomonic. Osler states that phantom tumors subside with a hissing sound. In 2 cases that I have observed for a long period this has not occurred. Metallic tinkling is heard in a dilated stomach, sometimes only after gently shaking the patient. It occurs in a colon dilated as a result of occlusion, particularly in case of carcinoma. It is always on the proximal side and indicates the location of the tumor. Thus, if heard on the right side, the tumor is at the hepatic flexure; if on the left side, it is at the lower end of the descending colon or in the Sigma romanum. Metallic tinkling is also heard in gas tumors that occur after perforation, and in these cases is almost pathognomonic. It occurs particularly if the collection of gas is limited and does not open into the general peritoneal cavity. It has been explained as the result either of drops falling upon the layer of liquid in the lower part of the tumor, or—and I think this more probable—of the bursting of bubbles of air in liquid.

Friction occurs in perisplenitis; of this I have observed one case. The friction was loud and similar to pleural friction. The pain was severe and increased by strapping, which, if usual, may be an additional point in the diagnosis. The spleen was palpable and tender. A friction rub is also heard in peritonitis, especially the tubercular form, and is not accompanied by pain. Occasionally it is heard in carcinoma, is loud and coarse, and usually, but not always, painless. Crepitation has been described in hydatid cysts, and is elicited by placing the bell of the stethoscope over the tumor and using gentle succussion.

Murmurs are very often heard in the abdomen, but not as frequently as the old textbooks would lead us to believe is a bruit heard over an aneurysm. Murmurs are frequently heard in the abdominal aorta in arteriosclerosis, in aortic regurgitation, in exophthalmic goiter, in severe anemia and in fevers. They are sometimes only elicited, and always made louder, by pressure. A murmur is sometimes heard over a cirrhotic liver, and a venous hum over the pregnant uterus. A systolic thud is occasionally heard over an aneurysm, and is common in aortic regurgitation, exophthalmic goiter and pernicious anemia. The heart-sounds are also at times

heard in the abdomen, but I have never been able to discover that their presence is related to abdominal tumors.

9. There are a few special palpatory features, independent of the general examination for the size and shape. Friction may be felt. I noted it in the case of acute splenitis and in several cases of carcinoma of the lower end of the stomach. I once felt crepitation in the gall-bladder, but although six stones were removed, the surgeon denied that I could have felt them rubbing against each other. Gersuny has described the Klebe symptom—a sudden separation of the hypertrophied colonic wall from a mass of feces as pressure is relaxed. It occurs only, as far as is known, in Hirschsprung's disease, and must be excessively rare, as no one else has described it. Gurgling may be felt in the colon on either side. A large gauze pad, although recognized as a foreign body, gave no particular sensation by which it could be recognized.

10. An abdominal tumor may, and usually does, cause displacement, the amount depending upon the size of the growth; it may, by pressure, affect adjacent structures and produce anemia or congestion, distortion, discoloration, obstruction. It may by its nature cause inflammatory or malignant changes, leading sometimes to penetration of the affected organs; it may alter profoundly the functional activity of the tissue.

The subject of displacement is beyond the scope of this paper. I may note as a useless but curious observation, that large abdominal tumors sometimes alter the electrocardiogram. They may cause the physical signs of consolidation to appear at the base of the lung. This I have observed in several cases of ascites on the left, and in a case of liver abscess on the right. If there is, as in the latter case, fever and leukocytosis, the differential diagnosis is difficult. On one occasion a phantom tumor, because of the increased intra-abdominal tension, produced a prolapse of the uterus. Anemia of tissue is rare as a result of tumor growth. Congestion may be observed in the spleen, as in liver disease, in the kidneys, the liver, and in the walls of the stomach and intestines, and in cardiac decompensation. Discoloration as a result of circulatory changes, passive congestion and polycythemia may be observed in the skin or, at operation, in the organs. Discoloration also occurs as a result of jaundice, pigmentation and infiltration by pigment-bearing tumors, such as the melanotic sarcomas. Obstruction is very common. Certain tumors grow within the veins and obstruct them

—the lymphangiomata that grow along the spinal column obstruct the lymph channels and may cause chylous ascites; any duct in the abdomen may be obstructed—the bile-duct, the pancreatic duct, the ureters or any part of the gastrointestinal tract.

Inflammatory tumors may produce inflammation in adjacent organs. Thus the inflammation of the left kidney may extend to the spleen; a diverticulitis may perforate into the urinary bladder; a carcinoma of the small intestine may extend to the adjacent stomach. The functional disturbance is often considerable; the liver, if the bile-duct is obstructed, may become an organ of internal instead of external secretion; the pancreas may lose its external, but retain its internal secretion; a kidney may cease to secrete altogether.

11. The general condition of the patient may suffer as a result of malignant tumors. Cachexia is a combination of anemia and starvation, usually terminating in a stuporous condition. It is justifiable to suspect malignancy if cachexia appears, and the diagnosis may be rendered more likely by the discovery of enlarged glands in other parts of the body. The tell-tale supraclavicular gland is rare.

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NOVEMBER 23

## A Histological Study of Testes from Syphilitic Patients

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(By Invitation.)

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It has been shown that Spirochæta pallida has a special predilection for the genital organs. Since Levaditi published his method of staining by silver impregnation, great interest has been aroused in the demonstration of spirochetes in tissues. This suggested a histological study of the seminal vesicles, testes, ovaries and inguinal lymph glands removed from syphilitic patients at necropsies. The study was also made with the hope of throwing some additional light on the conceptional transmission of syphilis, which is a widely discussed and important subject. The results of a similar study of the seminal vesicles has been published elsewhere.[1] At the suggestion of Dr. Schamberg this study was undertaken by me.

Materials and Method of Study. The report in this paper is the result of a study of testes from 40 syphilitic cases obtained from necropsies performed at the Philadelphia General Hospital. The blood or spinal fluid Wassermann reactions were positive during life in 25 cases. In 5, excluding the 4 stillborn cases, there was no Wassermann test made, because the patients died soon after admission. In the other 6 the Wassermann reaction was negative. These 15 cases are included because they either gave a positive history or clinically were considered as syphilitic, and because the tissues grossly and histologically showed syphilitic changes in conjunction with similar changes in other organs. The clinical diagnosis in the majority was some cardiovascular disease. In 5 each it was tuberculosis and hemiplegia and 4 cases were neurosyphilitic. The ages varied: 19 being over fifty, and thirty to fifty years, 16; 4 were stillborn fetuses with clinical evidences of congenital syphilis and 1 a three months' old negro baby with a strongly positive blood Wassermann reaction.

After examining the testes, sections were made for histological study. The fixation, staining and method of procedure used were similar to those applied in my study of the seminal vesicles.[1] The Levaditi method of silver impregnation stain was used for the search for Spirochæta pallida, since this method proved the most satisfactory in our hands. Two cases showing the greatest histopathological changes were especially studied for the presence of spirochetes.

In 8 cases an emulsion was made from the testes, seminal vesicles and lymph glands of each and injected into the testicles of normal rabbits. A dark-field examination for the demonstration of the spirochetes was negative for the emulsions injected. The rabbits were examined every week for four months, with negative results. The necropsies on human subjects were performed on an average of fourteen hours after death and the rabbits were injected about eighteen hours later.

Results. The gross appearance of the testes varied in the different cases. Some of them were normal, while others showed various degree of fibrosis. In 2 cases very little normal tissue was observed. Of frequent occurrence was a unilateral or bilateral hydrocyle. In none of them could a definite gross diagnosis of syphilis be made.

On the other hand, histologically, 23 cases showed some histopathological changes commonly attributed as a reaction to Spiro-

chæta pallida infection. The perivascular round-cell infiltration of plasma and lymphocytic cells was a marked feature. The degree of infiltration varied from a few cells to a large number. Another distinctive feature was the fibroblastic proliferation in the stroma between the tubules. Hyaline changes and fibrosis in some instances were quite marked. The bloodvessels showed some thickening. Of the testicular tubules some showed complete atrophy and fibrosis, while others only presented moderate changes. The basement membrane was thickened and as a rule there was diminished spermatogenesis. The cells of Sertoli showed moderate hypertrophy. These pathological changes were noted in both testes, but often more marked in one than the other.

The 2 cases selected for intensive study were clinically and histopathologically definitely syphilitic. One case was thirty-five years of age, with history of chancre at the age of twenty-five years. The blood Wassermann was 4 +, and there was no record of any specific treatment having been received. He was married for five years and his wife had one miscarriage with no other pregnancies. The sections presented a marked degree of perivascular round-cell infiltration of plasmas and lymphocytes with fibroblastic proliferation.

The other case was fifty years of age, with blood and spinal fluid Wassermann reactions of 4 +. The pathological diagnosis was paresis and syphilitic arteritis. The sections histologically showed the evidence of syphilis.

Neither in these 2 cases nor in any of the others was I able to demonstrate the presence of Spirochæta pallida though the control tissue of syphilitic fetus liver was positive in all cases.

In 1 of the 4 fetus cases, stillborn at the seventh month of gestation, the spirochetes were present in enormous numbers. Here the necropsy was performed twenty-four hours after birth. After the liver and testes were kept in the ice-box for three days a dark-field examination disclosed the presence of weakly motile spirochetes. This observation is of extreme interest because it showed that Spirochæta pallida in this particular instance did not die soon after death of the host, as is commonly supposed to occur. To carry our observations further, Miss Anna Rule, of the laboratory staff, inoculated rabbits intratesticularly with Spirochæta pallida and after the development of a syphiloma removed the testicles and placed them in an ice-box. The spirochetes were found to be alive

two weeks later. This finding justifies our technic of injecting emulsions from human tissues about thirty-two hours after death of the subject. In none of the rabbits inoculated with the emulsions were definite syphilomas demonstrable. Two or three days after the injections there was a reaction manifested by swelling, edema and in some cases ulceration of the skin. The glands were palpable in every instance. This reaction subsided gradually in all of them except 2, in which abscesses developed, due to secondary infection. A few drops of serum were removed by a syringe and needle, but dark-field examination proved them negative for Spirochæta pallida.

Discussion. It is a well-known fact that syphilis of the testicles is one of the most frequent manifestations of the disease. Though several monographs and numerous articles have been written on syphilis of the testes, there is still much discrepancy in regard to its frequency. Symmers,[2] in an analysis of 4480 necropsies performed at the Bellevue Hospital during a period of ten years, found anatomic evidence of syphilis in 314 cases, or an incidence of 6.5 per cent. Chronic interstitial orchitis was noted in 39 per cent of the syphilitic cases. Warthin,[3] in studying 750 necropsies performed at the University of Michigan Hospital, found evidence of syphilis in 300 cases, or 40 per cent of the total. In the later years the incidence was over 50 per cent. The presence of Spirochæta pallida was demonstrated by him in 75 cases. The testes showed syphilitic involvement in all of the 300 cases. The severity of the reaction was only secondary to that of the heart and aorta. This means that 1 out of every 2 that come into the autopsy room is syphilitic, or, in other words, 50 per cent of the hospital-class persons have had syphilis during their life. This seems to me to be an exceedingly high percentage. I have no accurate data as to the syphilitic percentage for the necropsies performed at the Philadelphia General Hospital, but I can safely say it runs about 8 per cent. According to my findings, 57.5 per cent of all the syphilitics showed pathological changes in the testes as a result of the Spirochæta pallida infection. This compares favorably with Symmers, who took into consideration mainly the gross anatomy, but it is much lower than Warthin's.

The fundamental pathological changes are perivascular round-cell infiltration of plasma cells and lymphocytes, connective-tissue proliferation and hyperplasia with hypoplasia of the parenchymal tissue. The latter phenomena may result from the connective-tissue hyperplasia or the toxins produced by the disease.

In 1916, Symmers and Wallace[4] stated that they examined thoroughly the viscera in 30 cases of syphilitic aortitis, and in none of these were they able to demonstrate Spirochæta pallida, with the Levaditi method. According to the same authors, Aschoff, Crowell and Brown had similar experiences. This is in contrast to the reports of Warthin, Longcope[5] and others, who were able to find them in the aortic wall in Levaditi preparations in about 25 per cent of cases. I was unable to demonstrate spirochetes in any of the cases except the stillborn fetus, although a thorough search was made in every one. According to personal communications from several of the leading pathologists in the city, I am assured that they have had similar experiences.

The absence of spirochetes from the tissue suggests the possibility of some morphological changes, in certain strains at least, after infection. A few observers have described a granular form of Spirochæta pallida, but these observations have been inconclusive. Whether or not the organism undergoes modifications or morphological changes in its life cycle, is a disputed question. Although such changes have not been demonstrated satisfactorily, it is possible that they may occur.

As early as 1876 Kossowitz[6] announced that, as a general rule, the degree of paternal transmissibility of syphilis to offspring gradually diminished in proportion to the duration of the disease. This statement is borne out by present-day observations and may partly explain the nondevelopment of syphilomas in the 8 rabbits injected by the emulsions of testicles in my experiments, as most of the testicles were derived from old individuals.

Summary and Conclusion. The testes from 40 syphilitic human subjects were studied grossly and histologically. In addition to the varying degrees of fibrosis there was, grossly, no characteristic changes. Microscopically, 23 cases, or 57.5 per cent, showed pathological changes commonly attributed to Spirochæta pallida infection. In 17 of the 23 cases the Wassermann reaction was positive, in 2 negative and in 4 not made. The Levaditi preparations were negative for the organism in all the cases except in a seven-month-old fetus, where the spirochetes were demonstrated in large number. Eight rabbits were injected, intratesticularly, with emulsions from 8 cases and observed for four months. None of the rabbits developed syphilomas. The findings in this study tend to show the frequency of the disease in the testicles and the difficulty of

demonstrating the organism in the tissues with our present methods and present knowledge of its morphology.

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## On the Production of Mydriasis in Rabbits by the Use of Thyrotoxic Serum and Adrenaline

BY ROBERT L. PITFIELD, M.D.

(*Abstract*)

It is conceivable that a toxic substance circulates in the blood of persons afflicted with toxic thyroid disease. This is of an unknown character if it exists, as it most probably does. The design of this communication is to establish by means of experiments in the eyes of rabbits that it is a chemical entity. That this substance is an irritant to the sympathetic nervous system probably accounts for the clinical signs present in toxic thyroid disease with or without exophthalmos. Serum from such patients was injected into rabbits and the effects upon their pupils noted. No mydriasis occurred. Adrenaline instilled into such injected rabbits intensively was followed by complete mydriasis in the eyes treated. The reaction occurred in varying intervals of time: It appears that the more toxic the patient, and the more nervous, the quicker would the mydriasis appear; also the less adrenaline would be required. It appears from the experiments performed that the toxic substance does exist, but the use of adrenaline as an adjuvant is necessary for the reaction to appear.

In 2 control cases without any hint of thyroid disease, serum and adrenaline instillations caused no mydriasis.

Two cases probably cured of thyrotoxic disease exhibited no reaction. In the controls and these cases, 1 cc of serum was used and 1 cc of adrenaline was instilled.

In 5 markedly toxic cases of thyroid disease, with and without exophthalmos, a marked reaction (mydriasis) appeared in varying periods of time and with less than the amount of adrenaline thought to be the most that was required to produce the reaction in toxic cases. Poisonous doses of thyroxin and adrenaline instillations as an adjuvant failed to produce mydriasis, of a complete character.

One rabbit succumbed after the injection of 5 mg. of thyroxin and the instillation of 1 cc of adrenaline. The animal lost weight rapidly, would not eat or move, its eyes were sunken and it evidently was in distress before dying. In 2 nontoxic enlargements of the thyroid no reaction was produced by serum and adrenaline instillations.

Instillation adrenaline alone did not cause any mydriasis of a paralytic nature. The eyes of the rabbits after the instillations appeared to be proptosed and the pupils slightly dilated, but they reacted to light promptly.

The serum from 1 very toxic case, which had produced the reaction in ½-cc dose, and adrenaline solution heated to 58 C. for 140 minutes, still produced mydriasis when ½ cc injected and adrenaline 0.25 cc was instilled in one eye of a healthy rabbit. From this one experiment it is inferred that the substance is thermostable.

A positive reaction requires that the following postulates be fulfilled.

1. One cubic centimeter of serum from a suspected case shall be injected into a healthy rabbit (white female rabbits were found to be the most sensitive).

2. Unless 1 cc of adrenaline 1 to 1000 is instilled into one eye of a rabbit injected with the serum, the reaction shall not be considered negative.

3. The mydriasis shall appear within ninety minutes, and the pupil shall not react in the slightest to the stimulus of a bright electric light held close to the cornea for a half minute.

4. The more toxic the case the more rapid will the reaction appear and the longer will it persist after the last instillation of adrenaline. Also the more toxic the case the fewer adrenaline drops will be required.

In some toxic cases the reaction appeared within forty minutes

and after the use of but 7 drops of adrenaline. Others not so toxic required 28 drops and the reaction was not complete until the lapse of sixty minutes.

Summary of Experiments. (*a*) Cases in which there was no mydriasis: Healthy individuals with no symptoms of toxic thyroid disease, 2; individuals in which the thyroid was the seat of a non-toxic enlargement, 2; individuals who formerly exhibited thyroid toxicity and were symptomatically cured, 2. Total 6.

(*b*) Cases of evident toxic disease of thyroid, with and without exophthalmos, 5. Total experiments on rabbits with serum, 11.

Since the reading of this paper 2 other individuals with toxic thyroid disease were examined by this method and a positive reaction obtained, making a total of 7 toxic cases with positive reaction.

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## The Final Solution of the Intracranial Pressure Problem

BY TEMPLE FAY, M.D.
(By Invitation.)

(From the Neurosurgical Clinic of Dr. Charles H. Frazier, University Hospital, Philadelphia.)

Early Methods of Treatment. The problem of dealing with cranial injuries was old even in the days of Hippocrates; but with his great work, *de Vulneribus Capitis*, we find the centuries that passed have added little to the knowledge and treatment of head injuries as so carefully described by him. Many of his observations are sound practices of today. His descriptions and recommendation for trephining have been followed almost to within the last decade; curiously enough, the very instruments he used are but little changed in style and construction, as listed by our modern instrument-makers, even though twenty-two centuries separate our day from his.

The care with which trephining should be undertaken, the areas of the skull selected, the thickness of the bony parts, the symptoms and prognosis of his cases, are shining examples of the problem which engrossed him and the solution of which has required over 2000 years to effect.

His great fear of trephining beneath the temporal muscle, because of the production of stupor, convulsions on the opposite side, and

death, were attributed by him to the great vulnerability of this muscle, because of its many nerves and its close connection with the brain, a belief that held sway and was echoed by Ambrose Paré, eighteen centuries later. He did not realize that the symptoms were probably caused by hemorrhage of the middle meningeal artery in the act of trephining or from the injury that led to the selection of this point for relief. He adjures his followers to leave this area strictly alone, else surely the above symptoms will develop.

His observations that patients, after a head injury, who showed bleeding from the ears and nose "frequently recovered," is a well-recognized fact today, the drainage of cerebrospinal fluid giving a natural form of decompression and cerebrospinal dehydration, though this was not recognized as the probable cause until very recently.

The use of loose dressings to injuries of the brain was advocated by him, so as to better permit the extrusion of the "harmful humors of the blood" and to allow pus to freely drain from the wound, else in its strict confinure the patient suffer from inflammation, convulsions and death.

Galen, three centuries later, did much to maintain these doctrines and practised their precepts.

We have in the works of Ambrose Paré the accepted methods of treatment in the sixteenth century, and indeed until quite recently they have seen little change or improvement. He was a close follower of the teaching of Hippocrates, but invented a more modern type of trepan, one which had a similar safety device for protection of the underlying structures as that seen in the Hudson drill, our modern instrument of today.

He devised many clever instruments to assist in his work of trepanning—a dural separator not unlike the present ones, drainage tubes and cannulus such as are now used for brain abscess—cautioned against trepanning under the temporal muscles and advocated stiptics to fungating brain substance with ligation of the stalk and amputation for protruding masses when local applications failed.

The treatment which concerns us particularly, in our modern phase of the problem, was his management of concussions and the control of intracranial pressure. He realized the brain became "engorged and inflamed" after injury, so he therefore practised extensive blood-letting from the longitudinal sinus, the frontal vein and the tongue. He applied heat and friction to the abdomen

to withdraw congestion from the injured parts, restricted his patients from the use of wine for fourteen days following the injury and advocated light liquid diet with *purgation*. This is so nearly our present method of treatment that if he had not had the infected wounds to contend with, due to his trephining, the results would have been more startling and impressive to his followers.

But before we could reach the present stage of our treatment, based on scientific experiment and physiological function, many discoveries were to be made which have lead up to the probable solution of the intracranial pressure problem. It must be borne in mind it was not until 1784 that Catugno discovered the cerebrospinal fluid, and over a century later, in 1891, that Quincke introduced spinal puncture. We shall see how the problems of head injuries today resolve themselves into (1) injuries, such as depressed fractures and hemorrhage, which demand immediate surgery for relief of the local conditions, and (2) head injuries, such as concussions with or without simple fractures of the skull, which demand primarily treatment for the relief of intracranial pressure.

Leaving out of the discussion cases of extensive brain damage when death is a matter of a few minutes or several hours, and those cases which require surgical intervention for localized hemorrhage or the removal of bone fragments, depressed or compounded, we have been aware that many head cases died after the local conditions had been relieved by operation or in the first twenty-four hours following a concussion from what was termed "medullary edema," "intracranial pressure" or, as is frequently heard, "The patient died of a fractured skull." It is obvious the latter condition was not the cause of death.

We shall now take up the more recent steps which have led to the solution of the problem which has concerned the followers of medicine through all the centuries.

Subtemporal Decompression for Relief of Pressure. Dr. Cushing perfected the technic of subtemporal decompression for the relief of pressure and was among the first to violate the dictum of Hippocrates, showing that the temporal muscle was in reality the safest point for removing the bones of the skull and incising the dura to permit expansion of the tense brain substance beneath the muscle offering the best protection against trauma and infection from without. This surgical procedure was devised for the purpose of allowing relief of pressure by displacement of brain volume into

the opening, and its results are in proportion to the requirements of the affected brain, it being evident that only pressure equivalent to the volume extruded was relieved. His technic and results received immediate recognition and have held sway almost to the present time. One surgeon, Sharpe, of New York, reports having performed over 1000 subtemporal decompressions for the relief of pressure, many as a precautionary measure against the possible occurrence of intracranial pressure following head injuries.

The majority of these cases were in children or young adults, leaving a permanent cranial defect. In the light of our present knowledge, it seems this method has obtained too radical an aspect to justify its performance simply as a preventive means where no pressure exists at the time.

It is evident, therefore, that the next step in the reduction of pressure was simply a method for increasing the size of the intracranial cavity temporarily to take care of the pressure phase, which usually lasted from one to seven days, following head injuries. Patients who survived this pressure following injury usually recovered. Certainly the subtemporal decompression has saved a great number of lives; but modern observations and methods have shown that this procedure is being confined now almost entirely to those cases where there is evidence of a focal lesion or hemorrhage in the region of the middle meningeal artery or to cases of brain tumor where some lasting means of relief must be considered.

Weed and McKibbon's Contribution in 1919. These two workers directed attention to the fact that injections of hypertonic solutions into the bloodstream, and also into the gastrointestinal tract, produced a marked fall in intracranial pressure as registered by a spinal manometer. They also pointed out that hypotonic solutions increased the cerebrospinal pressure. Following this contribution, which has marked the beginning of a new era in the treatment of intracranial pressure, Foley and Putnam verified their work and applied it to clinical cases on Dr. Cushing's service. It was soon advocated and used for the reduction of intracranial pressure, their method being the administration of 35 per cent sodium chloride solution intravenously. This produced a marked dehydration of the brain within a few minutes, and was used to reduce brain tension at operation where inoperable tumors, following an exploration, made closure of the dura difficult.

Haden, about the same time, administered hypertonic glucose

solution intravenously and obtained relief from intracranial pressure in a case of meningitis. Sachs, of St. Louis, also used sodium chloride solution intravenously and found that it relieved the edema of the brain at operation. Sodium chloride, as we shall see later, produces a rapid and effective dehydration for a few hours; but later, as shown by the work of Ebaugh and others, gave a secondary rise of intracranial pressure, probably because of the salt retention in the tissues themselves after the bloodstream had been relieved of its hypertonic state by elimination of the salt through the kidneys, fluid then passing back again to the tissues with even greater pressure symptoms than before. Ebaugh experimented at Johns Hopkins with the tambour placed over a subtemporal decompression opening, in a case of brain tumor with marked pressure. He demonstrated a fall in pressure, by diminution of the cerebral hernia and later a rise, with tension and bulging at the cite of decompression, following the administration of hypertonic sodium chloride, intravenously.

The Use of Magnesium Sulphate for the Reduction of Intracranial Pressure. In 1921, clinical observations on normal children at the University Hospital indicated that magnesium sulphate, when administered by mouth as a purge, caused retraction of the fontanel which was maintained until the child was sufficiently supplied with fluids to overcome the hydragog effects of the salts. It was evident that brain volume was reduced in a demonstrable way by the rapid elimination of fluid from the system through a hypertonic saline cathartic, such as magnesium sulphate. The observation was reported to Dr. Frazier and applied on the neurosurgical service, with the idea of reducing intracranial pressure, and was found to be effective in cases where pressure was due to or complicated by the presence of cerebrospinal fluid whose normal avenues of escape had been temporarily cut off. Its clinical application and effects have been carefuly studied during the past four years.

As has been stated, Ambrose Paré pointed out, in 1654, that purgation was of great value in cases of head injuries, and this became an empirical formula for many conditions. Hydrogogs have long been in use for ascites, edema and for the reduction of local swellings. The physiology of magnesium sulphate has long been known. Wallace and Cushny, Weed and McKibbon, Hay and many observers have established its properties. It is surprising its systematic clinical application for the reduction of intracranial pressure has been only recently established.

Dowman in 1922 and Weaver in 1925 have reported confirmatory results with magnesium sulphate.

An important property and much of its value lies in the fact that in proper dosage and under normal conditions magnesium sulphate is not a dializable salt. It therefore remains in the intestinal canal and draws fluid rapidly from the bloodstream, which in turn calls upon the free ventricular fluid to replenish blood volume, and thus secondarily reducing intracranial pressure. It was found to be an effective method for the reduction of intracranial pressure provided the patient received no fluid from outside sources during the period of dehydration. The application of this salt in the clinical work met not only the conditions found in brain tumor, but was found to control satisfactorily the pressure arising from intracranial trauma, without producing the disturbing secondary wave of pressure often fatal when sodium chloride solutions were used.

The effect of its administration has been confirmed by many workers and the results have been most gratifying. It was capable of relieving pressure more satisfactorily than the operative procedure and did not have the disturbing property of permitting a secondary rise in intracranial tension. It was found to be the ideal method of treatment in cases of pressure where the blood volume had not been reduced by either hemorrhage or shock ("surgical shock").

The index for its use, in a broad sense, may be considered as most effective in cases of head injury, brain tumor or meningitis where evidence of intracranial pressure exists or becomes manifest by headache, vomiting, failing vision or sudden falling respiratory rate, with or without a falling pulse-rate. The respirations in acute cases may be considered a fair index of intracranial pressure, and when below 20 indicate the need for dehydration. The pulse may be considered a fair index of blood volume. For instance, a pulse of over 120, following an injury to the head with evidence of shock, indicates an existing depletion of blood volume. This may be due either to actual hemorrhage from lacerations or the result of profound vasodilation with depletion of the available circulating fluids. Hence a pulse of over 120 should contraindicate the use of magnesium sulphate, for a concentration of the blood may occur, due to fluids rapidly becoming tissue bound or lost through profound sweating. This may be associated with a rise in hemoglobin concentration and a falling blood-pressure, especially the diastolic bed.

It is evident that in the presence of a depleted blood volume,

represented by a high pulse, hemoglobin concentration, leaky skin and low diastolic pressure, that to further deplete this blood volume by a process of dehydration through the intestinal tract, following the administration of magnesium sulphate, would only complicate the patient's condition, causing a further depletion in blood volume and probable death from vascular deficiency.

The addition of fluids by vein or mouth in a case of this kind, in order to make up the depleted blood volume and combat the shock, is indicated; but this, on the other hand, would only rapidly increase the existing intracranial pressure. It was, therefore, found that in this type of combined "shock" and "intracranial pressure" we faced a dilemma. The withdrawal of fluid from the bloodstream by the introduction into the intestinal tract of magnesium sulphate would only increase the shock, and increasing the fluid to offset the shock and reëstablish the blood volume would only manifestly increase the existing intracranial pressure. In this type of case, therefore, it became necessary to administer fluids rapidly by mouth or vein and to withdraw ventricular or spinal fluid to combat the intracranial pressure phase which followed in these cases. So that we still lacked a satisfactory means of medication which would meet the requirements in cases of severe intracranial trauma, though fortunately the majority of cases responded readily to the proper balance of dehydration and fluids through the use of magnesium sulphate. The final solution of the managment of intracranial pressure was only presented within the past ten months.

The Intravenous Use of Hypertonic Glucose Solution. Only last January, Dr. Howe presented the results of experimental studies, based on the work of Weed and McKibbon and many others, in the use of concentrated forms of glucose solution intravenously. He found that the administration of high concentrations of glucose intravenously caused a rise in blood-pressure and a fall in intraspinal pressure, probably due to the withdrawal of fluid from the tissues and especially a reduction in intracranial pressure by the depletion of cerebrospinal fluid volume. The free fluids rapidly enter the bloodstream because of the hypertonic state induced by the addition of glucose, and here they are maintained for a period of several hours. It, therefore, meets that type of case which has just previously been described, and solved the dilemma where shock and intracranial pressure exist simultaneously. It does this by adding

tissue fluids to the already depleted blood volume, and in withdrawing the tissue fluids it reduces the intracranial pressure, reëstablishing a vascular bed which approaches the normal, at the same time removing intracranial pressure which threatens the life of the patient. It is, therefore, with this final contribution that we may have means at hand to combat all phases of our intracranial pressure problem. Dr. Max Peet, in June, presented clinical confirmation of this work, which has also been verified by us and found to be most satisfactory in the small series of cases where its use has been indicated.

Surgery may be resorted to as a final means or repeated lumbar punctures performed if other means fail to reduce the intracranial pressure. It must be borne in mind that lumbar puncture may be dangerous in these cases due to increased intracranial pressure, and care should be maintained in withdrawing large amounts of fluid at any one time. This may be dangerous because of the possibility of cerebellar foramenal hernia with sudden death.

Summary. The old methods of trephining and decompression have been discussed and shown to be effective only to a limited degree. They are now confined especially to cases of depressed fracture and hemorrhage. The use of magnesium sulphate, by mouth or rectum, has demonstrated its ability to control intracranial pressure which is not complicated by shock in the combined picture of shock and intracranial pressure. We found the intravenous administration of 50 per cent glucose solution, as advocated by Dr. Peet, to be effective in combating intracranial pressure in the presence of shock. Surgery in these cases has become the method of last resort when other means of controlling the pressure have seemed inadequate.

In a series of 39 consecutive cases of head injuries since August 1, 1925, at the University, Polyclinic and Medico-Chi Hospitals, 24 sustained fractures of the skull, 18 being unconscious or confused for a period of one or more hours, the longest four days. There have been 5 deaths, a mortality of 13 per cent—1 death from pneumococci meningitis on the fifth day, 2 from massive collapse of the lung on the second and the tenth day, and 2 from pneumonia, one on the fifth and one on the ninth day following the injury. The management of these cases has been entirely by means of hypertonic solutions and without the need of surgical intervention.

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## Calcium Deficiency in Asthma, Hayfever and Allied Conditions

BY GRAFTON TYLER BROWN, M.D.
(By Invitation.)

In the past fourteen months, with the able assistance of Dr. Hunter, some 400 calcium determinations have been performed, 200 of them on patients of mine and a like number on normal individuals as controls. This report is based upon a painstaking analysis of these determinations. As I am specializing in the diagnosis and treatment of asthma, hayfever, eczema and allied conditions, all the patients referred to belong in this category.

Calcium Norm. Ionic calcium determinations on the blood serum of normal healthy individuals varied between 9.6 and 10.2 mgm. per 100 cc, with an average normal of 9.9 mgm. As a result of these findings we accepted anything below 9.6 as indicating a definite calcium deficiency. Readings from 9.6 to 9.9 (not inclusive) we prefer to classify as low normal. From 9.9 to 10.2 would be high normal and above 10.2 high. As no clinical significance has been attached to a high calcium content in asthma, hayfever, etc., throughout this report they will be placed in the same category with the normal and high normal determinations. In other words, any calcium determination of 9.9 or above will be called normal. We felt that this establishment of a definite norm for our technic was of fundamental importance.

Prevalence of Calcium Deficiency. In a series of 166 consecutive patients upon whom calcium determinations were made, 39 per cent had a definite calcium deficiency, 24 per cent were low normal and 37 per cent were normal. This clearly indicates that a considerable proportion of the type of patients under consideration have a definite calcium deficiency.

*Asthma.* There were 100 patients with asthma. Of these 42 per cent had a definite calcium deficiency, 23 per cent were low normal and 35 per cent were normal. In this group are included both asthmatic bronchitis and true bronchial asthma.

*Perennial Hayfever.* There were 43 patients with perennial hayfever or hyperesthetic rhinitis. Of these 37 per cent had a definite calcium deficiency, 21 per cent were low normal and 42 per cent were normal.

*Seasonal Hayfever.* There were 32 cases of typical seasonal or pollen hayfever. Included in this group are spring, summer and fall types. Of these 28 per cent had a definite calcium deficiency, 34 per cent were low normal and 38 per cent were normal.

*Eczema.* There were 15 cases of eczema in our series. Forty per cent of these were calcium deficient, 20 per cent were low normal and 40 per cent were normal.

*Protein Sensitization.* In the series of 166 consecutive patients previously referred to there were 68 who gave one or more definite positive reactions on cutaneous tests with various foreign proteins, 22 who gave slight or doubtful reactions and 76 who gave no reactions whatsoever on skin tests. The relative proportion of protein sensitive cases in this series is much smaller than in my average run of patients. This is due to the fact that calcium determinations were not usually made on those patients who were frankly protein sensitive, as the diagnosis and treatment of these cases was clear cut, *i. e.*, elimination or specific protein desensitization or both.

Of the protein sensitive cases in this series 37 per cent were calcium deficient, of the protein doubtful group 41 per cent were deficient and of the protein negative 39 per cent. According to these figures no relation exists between protein sensitization and calcium deficiency.

Treatment. All patients with any degree of calcium deficiency were advised to eat plenty of the foods that are rich in lime and to get as much sunshine as possible.

Patients with a low normal calcium were all given calcium lactate,

and parathyroid or thyroid or both, by mouth. Patients with a definite calcium deficiency were given the same, with the addition of quartz-lamp treatments.

*Calcium Lactate.* The dose of calcium lactate was from 3 to 10 gr. three to four times a day, about one-half hour after meals, the average adult dose being 5 gr. three times a day. It was prescribed in tablet form to be broken up in half a glass of water.

*Parathyroid.* The dose of parathyroid was from $\frac{1}{20}$ to $\frac{1}{10}$ gr. in tablet form, two to four times a day, with or after meals, usually taken at same time with calcium lactate, the average adult dose, being $\frac{1}{20}$ gr. three times a day. For routine administration in calcium deficiency I much prefer parathyroid to thyroid. According to the work of Grove and Vines the parathyroid glands are the chief regulators of calcium metabolism in the human body, so parathyroid substance would seem to be the logical thing to use in calcium deficiency cases. Also parathyroid seems to have no contraindications to its use, whereas thyroid is definitely contraindicated in some cases.

Results. The treatment just described for correction of calcium deficiency was given to 101 patients, and of these the results are known in 94 cases. . . Gratifying results were obtained in 54 per cent of the calcium-deficient cases, definite improvement in an additional 43 per cent and in only 3 per cent of the cases was the treatment a failure. However, these good results cannot be attributed solely to the correction of calcium deficiency as other therapeutic indications were taken care of whenever they occurred, such as elimination of offending proteins, specific protein desensitization and the use of autogenous vaccines. Nevertheless, I am convinced from my observation of the patients under treatment that the correction of calcium deficiency was of invaluable assistance in handling these cases. Furthermore, in some of these cases relief or "cures" were obtained by the correction of calcium deficiency alone, without any other form of treatment.

Patients usually report an increase in "pep" and energy, and a general feeling of well-being, as a result of the correction of calcium deficiency.

Conclusions. The establishment of a definite calcium norm for the individual laboratory technic is of fundamental importance.

A considerable proportion of all cases of asthma, hayfever, eczema, etc., have a definite calcium deficiency.

No relationship exists between the incidence of calcium deficiency and any of the following factors: sex, age, protein sensitization, duration of disease or eosinophilia.

Calcium deficiency is entirely correctable by the methods at our disposal, namely, calcium lactate, parathyroid, thyroid and quartz-lamp, and in a number of cases fixation of calcium seems to have been accomplished.

The detection and correction of calcium deficiency is not offered as a substitute for protein sensitization work, but is a valuable addition to the well-known and accepted methods of treatment in asthma, hayfever and allied conditions.

# PROCEEDINGS

OF THE

# SECTION ON PUBLIC HEALTH AND INDUSTRIAL MEDICINE

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MARCH 13

## The Prevention of Scarlet Fever

BY JAMES C. SMALL, M.D.
(By Invitation)

An intelligent prevention of an infectious disease, as well as its treatment, must depend on definite knowledge of its cause. The cause is a living microscopic agent, which differs for the different diseases, but usually belongs to the group of organisms known as bacteria. These bacteria usually invade the host in which they produce disease through some very definite portal of entrance. For our purpose tonight we will consider only those microörganisms which gain entrance through the nose and mouth and find lodgment in the upper respiratory passages. Such bacteria are most commonly transferred from person to person through the medium of "droplet spray" of the upper respiratory secretions scattered broadcast by the infected individual in acts of sneezing, coughing or talking, and are breathed in by the next individual in whom they are to produce disease. One may call this direct aërocontact transmission. Upon implantation on the surface of the membranes lining the nose and throat the first requisite in the production of disease is the ability of the virus to reproduce and multiply in this location; the next is its ability to invade the tissues. This property of invasion is spoken of as virulence of the microörganism and differs for different bacteria. Immediately the microörganism begins to invade the tissues the body defences against such invasion are

called into play. If these body defences are successful in resisting the invasion of the microörganism, its implantation in that particular individual is incidental and passes unnoticed because no noteworthy symptoms are produced. If, however, the body defences are not prepared to combat successfully the invasion of the microorganism, serious manifestations of such invasion result. Some types of bacteria are aided in their attack upon man by a property which they possess upon growth of producing a powerful poison or toxin which paralyzes the individual's forces of resistance to the invasion. Some individuals have already in their blood an antitoxin which serves to neutralize this toxin of the bacteria. In these individuals the invasion of the bacteria is successfully resisted, and the individual is spoken of as immune to the infection. Those who do not have this antitoxin are spoken of as susceptible to the infection.

Some bacteria which produce these toxins when they grow naturally in our tissues, may be grown artificially in the test-tube under conditions whereby they produce the same toxin. Given such a toxin in the test-tube for a particular disease, we can use it for three purposes in combating the disease: (1) We can inject very minute amounts into the skin of normal individuals and obtain definite knowledge from the nature of the trifling local reaction which follows as to whether the individual is or is not susceptible to the disease in question. (2) After having determined in a group of individuals those which are susceptible to the disease, we can by using injections of larger amounts of the toxin excite the production of antitoxins in the blood of such individuals so that they are no longer susceptible to the particular disease. (3) We can inject animals with repeated doses of the toxin and obtain in the blood serum high concentrations of antitoxin. The serum from such animals can then be preserved and used in neutralizing the toxins which happen to be producing serious acute illness in a given individual.

Bearing these general principles in mind, let us consider more specifically how they apply to scarlet fever. It appears obvious that their application must depend upon our knowledge of the specific bacterium causing scarlet fever. This has been the riddle of scarlet fever which was solved only recently. Scarlet fever was known to the medical profession for many years before the era of bacteriology made it possible to search for a specific microörganism as its causative agent.

The first unmistakable account of scarlet fever was by Daniel Sennet, of Wittenberg (about 1625); but it was Sydenham, in 1675, who gave the first full account of the disease under the name, *Febris scarlatina.* Common in Europe during the eighteenth century, it appeared in North America, according to Craigen, in 1735, spreading throughout New England, thence to New York in 1746. With the beginning of the era of bacteriology, in the nineteenth century, interest was aroused in a search for the causative bacterial agent. Certain bacteria (streptococci) were associated with the sore-throat of scarlet fever almost from the first. Streptococci were, however, found in association with many other abnormal conditions not at all akin to scarlet fever. Confusion therefore arose, and since it was not then appreciated that there were many kinds of streptococci, all resembling one another very closely, it came to be doubted whether the streptococci actually found were the real primary causative agents in scarlet fever, or whether they were simply concomitant agents causing certain of the complications of the disease but not actually instituting the disease itself.

A ray of light was shed upon the real cause of scarlet fever in 1902, when Moser and von Pirquet, using streptococci isolated from patients with scarlet fever, prepared in animals a serum which in their hands yielded very hopeful results in the treatment of scarlet fever. There can be little doubt that the nature of the disease was almost discovered at this time. Several other workers confirmed these good results with serum; but very shortly a number of others failed with serums prepared after the method of Moser, so that after a period the matter of a specific action of a streptococcus serum in curing scarlet fever was dropped.

The idea of a filterable virus, *i. e.*, an organism too small to be seen by the ordinary microscope, came to be more or less popular as an explanation of the causative factor in scarlet fever.

The next important contribution bearing on the cause of scarlet fever was made by Miss Tunnicliff, in Chicago, in 1902, when by complicated laboratory procedures she showed that the streptococci occurring so constantly in the throats of patients with scarlet fever constituted a particular group, and that the members of this group, while similar one to another, differed from the streptococci derived from sources other than scarlet fever. She showed, further, that patients with scarlet fever early in the course of the disease

possessed little power to fight off infection with this particular streptococcus, but that during convalescence they possessed this power to a greater degree than normal individuals. This important contribution did not at the time receive the attention which it deserved, largely due to our heritage of misconception in regard to the cause of scarlet fever. In 1918, the observation was made that convalescent serum possessed the property of blanching the rash of scarlet fever in a local area about the site of an injection of it into the skin (the Schultz-Carlton phenomenon).

From this on the work which has led to our present conception, and what is without doubt the true conception of the nature of scarlet fever, culminated very rapidly. Two groups of workers were concerned in bringing about the solution of the riddle of scarlet fever: The eastern group, composed of Dochez, Avery, Lancefield, Bliss Sherman and Blake, and the midwestern group, Drs. George and Gladys Dick, working in Chicago.

The contributions of the former group consisted of the development of better methods for differentiating different strains, the confirmation by this method of the occurrence of a particular variety of streptococci in scarlet-fever patients, the development of a specific serum for treating patients suffering from scarlet fever and the demonstration of the curative effects of this serum in the treatment of such patients.

The work of the Dicks stands out as epoch-making because of two things: (1) They appreciated the fact that the real reason for lack of progress in the solution of the problem was the lack of susceptibility of experimental animals to inoculations with scarlet fever. They, therefore, departed from the beaten course in experimental work and used humans for inoculation purposes. In doing this they were the first to show that the streptococcus from scarlet-fever patients produced this disease when inoculated into susceptible humans. (2) They produced in the test-tube the toxin elaborated by these streptococci, and with this toxin once in hand they developed a skin-test enabling one to pick out susceptible individuals from those not susceptible to scarlet fever; they produced symptoms resembling those of scarlet fever by the injection of proper doses of this toxin alone; they were able to show that susceptible individuals can be rendered nonsusceptible by the use of injections of this toxin and that an antitoxin could be prepared in the blood of animals which could then be used in neutralizing the toxins causing the acute attack of scarlet fever.

The present conception of scarlet fever, then, is that it is caused by a streptococcus growing usually primarily in the throat, where soluble toxins are produced and diffuse outward to give rise to grave general symptoms. The complications and sequelæ are partly due to residual effects of the grave toxemia and partly due to invasion and local development of the bacteria in points adjacent or far removed from the initial site of the infection in the throat.

Barring complications of the latter type the streptococci disappear rather rapidly from the throat in most instances. If they invade the accessory sinuses, the middle ear, the glands of the neck, etc., the organisms persist for long periods; in fact, such individuals may become permanent carriers of these bacteria and at any time serve as the medium for infecting others. Individuals who are immune to scarlet fever may, when in contact with acute cases of the disease, for a time harbor these organisms in their throats, presenting either no local symptoms or only mild local signs of inflammation. These may be called contact carriers.

The acute carrier, *i. e.*, the patient with scarlet fever, is the chief source of danger in the spread of the disease. The permanent carrier and the contact carriers are the other sources of danger, chiefly important because they frequently go unrecognized and thus serve in maintaining the endemic characters of the disease.

This rapid transfer from susceptible individual to susceptible individual is important in that it seems to increase the virulence of the organism. It may, in large part, account for the great variations noted in the severity of different epidemics of scarlet fever.

In the prevention of such a disease as scarlet fever there are two general plans of attack: The first includes measures taken to prevent the spreading of the causative agent, and the second includes measures taken to render susceptible individuals nonsusceptible to the disease.

The first has heretofore failed to eradicate the disease, although it has been to a certain extent instrumental in controlling epidemics. Greater success with these methods is not likely to eradicate the disease even now with our better understanding of the nature of the causative agent.

The logical point of attack, where failure to control the spread of the streptococcus is admitted, is that of rendering susceptible individuals immune to the infection. Many individuals are naturally immune and therefore need no treatment.

The skin-test made with the toxin of the streptococcus of scarlet fever, known as the Dick test, enables the identification of those who are likely to be attacked by the disease given the opportunity for contact with it. This class of individuals varies from roughly 20 per cent to 80 per cent of given groups, varying widely with the age and the opportunities for previous exposure to the disease. Children show higher percentages of susceptibles than do adults; children of the well-to-do higher percentages than children of the poorer classes.

Having determined susceptibles, these are rendered immune by the injection of graduated doses of the toxin, beginning with not more than 100 times the dose employed for the skin-test for the first dose; repeating with $2\frac{1}{2}$ times this dose after a week; and giving still a third dose of from $2\frac{1}{2}$ to 5 times the first amount used.

Now you will naturally ask, is not all this so new that it is really yet in the experimental stage? Yes and No!

The Dick test, followed by immunization of those shown to be susceptible, has been practised upon thousands of individuals, notably by Zingher in New York. Both procedures have been shown to be reliable and efficient. Naturally it may be expected that the present practice in the application of these principles does not represent final perfection. Difficulties are to be expected in any complicated biological procedure. One outstanding difficulty in this procedure is the matter of accurately measuring the strength of the toxin in the products to be used. At present the strength of the toxin is measured in terms of the amount that will produce a certain type of reaction when injected into the skin of known susceptible individuals volunteering for this purpose. It is obvious that this does not permit of as accurate an estimation as would be desired. We need to know more about technical matters in the production of this toxin. Again, it must be expected that considerations other than enthusiasm for the prevention of scarlet fever may place on the market inferior products for this work. The public is protected in such matters by certain standards imposed by Federal law and there is little doubt that adequate supplies of reliable products will soon be available.

The big task which faces those interested in preventive medicine in this matter is the application of these methods in communities of individuals. The discovery of a law or of principles beneficial to a community does not in itself benefit the community. It is the application which benefits.

Some one has said that one of the difficulties with constitutional government is "that governments move on, while constitutions stand still." More and more in these days of preventive medicine do we find its progress hampered by our code of medical ethics, which has not been revised to meet the needs of preventive medicine. Preventive medicine needs ways and means to parade its "stock in trade" before the public eye. Medical societies should take a lesson from modern business corporations. The radio business was not built up so quickly to present proportions through public meetings and personal appeal. Certainly people desire health more than they long for a radio apparatus, if they are only made to realize it. They can be made to realize it by the use of proper appeal from medical societies through the medium of the press. This appeal should give definite instruction in the benefits from the practice of these principles; should show the failures of methods formerly practised; should specifically direct individuals to their family physicians; should give them an idea of the relative insignificance of subjecting themselves to the procedures and give some approximation of the expense involved. Most important of all, such appeals should be repeated daily for long periods and properly placed in the advertising columns of the newspapers.

The educational program which has been employed in connection with diphtheria prevention should aid in this program for prevention of scarlet fever. The methods of arousing interest in both of these important procedures should, however, be changed, especially since those employed in the diphtheria work cannot be called highly efficient.

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## The Need for More Intensive Effort in Diphtheria Prevention

BY EDWARD L. BAUER, M.D.

Since the day that diphtheria antitoxin assumed an undisputed position as a specific remedy for diphtheria, a feeling of security in this remedy has brought about a situation that amounts almost to carelessness, or at least leads many people, including physicians, to regard diphtheria contemptuously.

For a period of from five to ten years following the introduction

of antitoxin for curative purposes, there has been a rather slow but vacillating decline in the mortality-rate. Then the decline was rather sharp, and for the last few years it has been down to what we regard as a minimum, at about 14 to the 100,000. The incidence of the disease, however, while it has fallen off somewhat, gives us no satisfaction in results accomplished or attained by preventive measures thus far employed. Economically there has been no decrease in expenditures necessary to care for the diphtheria sufferers in our community for the last ten years, for the per capita cost per patient more than overbalances a slight decrease in the number of cases that have occurred.

The use of antitoxin as a preventive measure in exposed individuals and the strict isolation of cases have helped to keep the diphtheria incidence down to a certain extent, probably even keeping it from assuming epidemic proportion at times, and these measures must certainly not be abandoned. Not so much can be said for the help gained from the standpoint of taking cultures, to prevent the disease by isolating carriers. The comparative ease with which the organism can be isolated led many epidemiologists to the conclusion that by means of wholesale culturing carriers could be run down. No large city in the United States worked out a system of culturing or carried out a plan with greater finesse than the city of Philadelphia. Here every known contact with a case of diphtheria was cultured, and if the organism was recovered the indivldual was isolated until he had received two negative cultures taken on successive days. Two negative cultures were required under the same conditions on every patient. Extensive cultures were made in schools where diphtheria was found and still we had diphtheria at the same old incidence rate. For the last six months the two negative cultures on the patient for termination of a case and a negative culture from the nurse is all that we have asked, with no deleterious changes in our incidence.

Scrutinizing carefully just what has been accomplished by the wholesale culturing, much could be learned. The sum-total, however, seems to show that the desired end is rarely attained by means of cultures. Only occasionally is a carrier found who is a menace to the community and the importance of this find is so far overshadowed by those not found, even by wholesale culturing, that it presents the picture of chasing rainbows when we concentrate our attention upon this carrier. Another thing has made itself

apparent in the use of cultures, that is the tendency to withhold diagnosis and treatment in doubtful cases while awaiting its result. This has increased the length of time in which the disease has gained headway before treatment is instituted in a proportion of cases that is distinctly noticeable in our incidence and mortality table, and it always works to the detriment of the individual.

DIPHTHERIA SINCE 1888 IN PHILADELPHIA

| Year. | Cases reported. | Deaths. | Case death-rate. |
|---|---|---|---|
| 1888 | 1170 | 623 | 53.2 |
| 1889 | 1455 | 727 | 50.0 |
| 1890 | 1820 | 943 | 51.8 |
| 1891 | 3251 | 1362 | 41.9 |
| 1892 | 5051 | 1707 | 53.8 |
| 1893 | 3471 | 1159 | 53.4 |
| 1894 | 3608 | 1395 | 38.7 |
| 1895 | 3853 | 1349 | 35.0 |
| 1896* | 3595 | 1155 | 32.1 |
| 1897 | 5405 | 1474 | 27.3 |
| 1898 | 4415 | 1154 | 26.1 |
| 1899 | 4391 | 994 | 22.6 |
| 1900 | 5088 | 1042 | 20.5 |
| 1901 | 3588 | 643 | 17.9 |
| 1902 | 2444 | 515 | 21.1 |
| 1903 | 3043 | 608 | 20.0 |
| 1904 | 3546 | 541 | 15.3 |
| 1905 | 3238 | 452 | 14.0 |
| 1906 | 3707 | 546 | 14.7 |
| 1907 | 3840 | 509 | 13.3 |
| 1908 | 3863 | 495 | 12.9 |
| 1909 | 3878 | 512 | 13.2 |
| 1910 | 3804 | 492 | 12.9 |
| 1911 | 3792 | 498 | 13.1 |
| 1912 | 3080 | 388 | 12.6 |
| 1913 | 2623 | 359 | 13.7 |
| 1914 | 2610 | 329 | 12.6 |
| 1915 | 2613 | 317 | 12.1 |
| 1916 | 2499 | 390 | 15.6 |
| 1917 | 3141 | 441 | 14.0 |
| 1918 | 2477 | 384 | 15.5 |
| 1919 | 3763 | 445 | 11.8 |
| 1920 | 3368 | 413 | 12.2 |
| 1921 | 3382 | 318 | 9.4 |
| 1922 | 3069 | 281 | 9.2 |
| 1923 | 3310 | 270 | 8.1 |
| 1924 | 3874 | 275 | 7.1 |

* The dispensing of antitoxin began in 1896.

One other evidence of the failure of wholesale culturing to assist materially in reducing the incidence of the disease is the parallel case of scarlet fever. There is no doubt about the parallelism of

these two diseases. Obviously there are scarlet fever carriers just as surely as there are immunes and nonimmunes, and we have not had any cultural methods to assist us in controlling the spread of scarlet fever. Zingher says, too, that the degree of susceptibility to scarlet fever is approximately the same as that in diphtheria, and if this is true why is our scarlet fever incidence rate regularly below rather than above our diphtheria rate, except in an occasional year?

Death-rate per 100,000: 1923, 14; 1924, 14.1.

It seems apparent then that we have reached a point of maximum results from a preventive standpoint in methods used, and some explanation must be made for decreases in incidence and consequent mortality rates enjoyed by other cities and not yet apparent in our figures. Take, for example, the city of New York. They have never indulged the culture as it has been done in Philadelphia, and our figures until within the last two or three years have run parallel. Now they show a precipitous decline and we our usual gradual one. This is obviously due to an increasing immunity rather than an attempt to catch carriers, transient or otherwise. Park claims that 700 lives have been saved in the city of New York because of active immunization against diphtheria, and his decrease in incidence and mortality in that city bears him out.

Active immunization against diphtheria by means of toxin-antitoxin mixtures is developing an immune population in New York City out of all proportion to any previously known degree of immunity to diphtheria, and this will undoubtedly be read in New York tables indelibly as the work is sustained. True, enthusiastic claims have been made in the past for other procedures. When antitoxin was discovered, enthusiasts immediately said that the last word had been spoken; but we learned the temporary nature of the immunity conferred by antitoxin and set out to discover other means. Chasing the diphtheria bacillus has proved a will-o'-the-wisp from the wholesale standpoint, and on second thought would be of value only if there was never intercourse between communities. Immunity, therefore, offers us our only solution, and an immunity that is permanent or nearly so.

Large groups of individuals have been reported from time to time in the last five years as having been immunized by means of toxin-antitoxin, and in these large groups diphtheria has not occurred. In groups of individuals given toxin-antitoxin, 95 out of every 100

should show at the expiration of six months an immunity to diphtheria. Never should this immunity be certified to, however, until the individual has proved the immunity by showing a sufficient blood antitoxin content to confer immunity. This can be most expeditiously demonstrated by the Schick test. The 5 per cent remaining may still be immunized by further injections. Again, groups showing an immunity following the use of toxin-antitoxin administered years ago still show their immunity with an increased blood antitoxin content at the end of eight years.

In the light of evidence at hand where hundreds of thousands of children have been immunized against the disease, it behooves us to immunize our population as far as possible. In approximately 100,000 children immunized by the Department of Public Health of Philadelphia against the disease under my supervision, there have been no deaths from diphtheria. This covers a period of from one to six years, as compared to a death-rate of 14.1 per 100,000 in one year, at least 30 per cent of whom were naturally immune. This is the same state of affairs that can be cited by Park and Zingher in at least 750,000 children in New York City.

The details of active immunization and Schick-testing have been presented to the physicians so frequently in the last five years that it would be trite and probably boring to enter into a lengthy discussion of that phase of the subject at present; but the fact remains that in this community at least the physicians have been slow to recommend the procedure and a far too large a proportion show a crass ignorance as to what it is all about. This is indeed unfortunate, and means that unless this condition is promptly remedied the Department of Health will be called upon morally to take the matter entirely into its own hands and intensively strive to effect a high degree of immunity in our population.

Economically and epidemiologically, a reduction in diphtheria incidence and mortality will be in direct proportion to the degree of immunity that exists in a given community, and in the future the incidence and mortality will be measured in inverse proportion to the intelligence of the community and the activity of its medical profession in developing this immunity.

## DISCUSSION

Dr. Wilmer Krusen: I do not intend to discuss this subject so much from the scientific as from the statistic standpoint. I sincerely hope that the optimism will be borne out in increased interest in industrial medicine. The people to whom we want to have this message given by Dr. Small and Dr. Bauer are not here. They were invited. Sir George Newman, chief medical officer of Great Britain, in a communication says: "Just as long as public-health knowledge is esoteric or exclusive, and does not filter down through the masses of the people, it is ineffectual;" and that has been demonstrated to my mind by the statements made both by Dr. Small and Dr. Bauer.

I have been preaching, teaching and sending out bulletins, and by various public-health talks over the radio and in many other different ways trying to educate the public to the possibilities of immunization from diphtheria. There is no reason in my mind that diphtheria should not be placed in the same category as smallpox in the city of Philadelphia. We know that we can prevent it.

From 1905 to 1924 there was not a single death from smallpox in the city of Philadelphia. Since January 1, 1925, there have been 3 deaths. Are we lacking in vigilance? Are we preaching vaccination? Is the family physician practising as he ought to? Dr. Cairns will tell you, when he discusses the subject of smallpox, that a great many of these cases are preventable. Sometimes we get lulled into false security by the absence for so many years of any outbreaks of smallpox.

Statistics are I know uninteresting, but take the question of scarlet fever: We had last year 42 deaths from scarlet fever as against 485 deaths in 1892. Now the immunization of scarlet fever is not quite in the same degree of development or certainty as diphtheria, and you see how careful public health officials have to be that any biologic product which is used for immunization must be standardized. If any accident occurs, then the poor health officer gets the blame for it. I am hoping there will be a standardized product for immunization. It is for the laboratory man to tell the family doctor how soon he has a safe biologic product that can be used without danger. We are optimistic; only a few years ago the campaign against tuberculosis was inaugurated; in 1880 there were 317 deaths per 100,000 population from tuberculosis, so I believe we can look forward to a sufficient quantity of biologic product that will aid us in the treatment and reduction of mortality in scarlet fever.

In diphtheria, with a remedy in our own hands, the mortality dropped through the use of antitoxin, and now that we can prevent the disease by the use of toxin-antitoxin it is really amazing that physicians have not taken advantage of this measure to the degree we have a right to expect.

Now it is rather humiliating, I think, for the family doctor to be told by the mother or father of a group of children: "Doctor, why don't you protect my children as Dr. Bauer or Dr. Jones has protected my neighbor's children?" What more can your health officials do to educate and stimulate the profession to avail themselves of the remedies which are just as valuable

as vaccination against smallpox? We want efficiency to be the slogan of this administration. I do not know whether you have felt it as keenly as I have: it has been a source of great regret to me not that New York has done such splendid work, but that we have not equaled New York in our work.

Dr. J. Claxton Gittings: If so many people after all these years are willing to forego the benefits of vaccination, especially after all the publicity in the papers this winter, it is not hard to see why we have difficulty in introducing diphtheria toxin-antitoxin. Apparently people will not become excited about future ills. The present is the only time that concerns them and if they are willing to take a chance with such a disease as smallpox, they certainly will be all the more apt to do so with diphtheria. I am accustomed to speak about the toxin-antitoxin to all my patients, so that they will at least know about it, but I find that most intelligent people have heard of it. Failure to make use of it is certainly not due to ignorance of its existence. In a number of cases I find parents opposed to it because of supposedly ill-results following its use. The three most prominent instances of this were cases of cyclic vomiting starting a few hours after inoculation. I have never been able to find any one who could explain the possible relationship between inoculation and attacks of vomiting. Possibly it was nothing more than a coincidence, but it certainly had a deterring effect upon parents who heard of it.

With regard to physicians, the greatest difficulty seems to be due to apathy. Another reason is the uncertainty in interpreting the Schick test. Again it may be due to a fear of the consequences, as anything which happens to patients within a week or two after the injections is apt to be blamed on them and this ill-natured gossip among a certain class of patients is feared by many physicians. The last objection, of course, is not a sound one and there were many instances of withholding the use of antitoxin years ago for the same reason. With the increased practice of immunizing children against diphtheria, however, the fear of possible ill-effects will diminish.

The difficulty in making and interpreting the Schick test is a real one. It is possible that the board of health will have to assume responsibility for the final Schick test. Two of the most telling arguments that I have used for inducing patients to have their children immunized are that successful immunization against diphtheria practically precludes the possibility of a tonsillitis proving to be diphtheria. In most cases that show patches on the tonsil the physician feels it is necessary to take cultures and sometimes even to use antitoxin while waiting for the report. If the child has been immunized this anxiety and unpleasant experience would be prevented. The other argument concerns the difficulty in differentiating a severe attack of croup from laryngeal diphtheria. It is obvious that an immunized child in all probability would not develop laryngeal diphtheria no matter how severe the obstruction. Freedom from anxiety on this score is certainly very greatly to be desired.

Dr. Randle C. Rosenberger: In speaking of smallpox, it appears to me that the only way to control the disease is compulsory vaccination. To prove this one would only have to glance at the incidence and mortality from smallpox during the Russo-Japanese war and the Franco-German war.

During the last twenty-five years, the incidence of the disease in Germany has been almost *nil*, due to the compulsory vaccination statute.

In England for a long term of years the nation was free of the disease, but on account of this freedom the bars were let down and the practice of vaccination was not enforced. Consequently the later generations developed the disease and smallpox is quite common.

The Philippine statistics have been referred to many times, and when the practice of compulsory vaccination was actually enforced smallpox disappeared.

Two things I insist upon in my course of lectures on preventive medicine: Where you see a suspicious throat inject antitoxin of diphtheria; and second, teach and practice compulsory vaccination against smallpox.

Dr. Seneca Egbert: There is an article in *The American Public Health Journal* for February in regard to the work done in Auburn, New York, a city of 36,000 people, detailing how they have practically eliminated diphtheria from the school population within about three years and practically immunized the whole child population. If that can be done in a city of 36,000 in three years it seems to me we might take certain localities in this city and do the same thing. I do not want Dr. Bauer or the health department to feel that we think they are not doing indispensable work. But it seems to me if we can divide the city into small sections and carry on some of this work intensively as missionaries and get busy driving this thing home to the minds and conscience of the rest of the profession and if we will go after everybody in a section just as Dr. Cairns has gone after everybody in a quarantined block in this smallpox epidemic, it seems that much might be done and that this is one way in which it could be done. If we could in a short time prove that a given neighborhood is entirely clear of this disease it would be an object lesson to the surrounding districts and it would not then be so hard to get the whole city to come across. We need the sort of intensive antidiphtheria campaign, such as Dr. Cairns has carried on against smallpox, intensive especially as to the lowering of the death-rate in infants and children.

Dr. Bauer (closing): The case of cyclic vomiting that Dr. Gittings quoted was called to my attention by telephone shortly after its death. I immediately got in touch with the state health authorities in whose jurisdiction the case belonged and their report to me upon autopsy was that the child had died of a gastrointestinal condition entirely foreign to its toxin-antitoxin injections.

There are but two things that might happen that would cause alarming symptoms or accidental death following the use of toxin-antitoxin: In the first place a reaction to the protein content might result, and since this content has been reduced to a trivial entity no danger need be feared from

that standpoint; or the reaction might be due to the only other potent ingredient, that is a reaction to diphtheria toxin. If the toxin is in excess, then the toxemia of diphtheria will manifest itself. If the protein is practically absent, as it is in properly made products, and the toxin is in properly gauged and regulated dosage, then nothing will happen. Certainly not the far-fetched and fantastic conditions so frequently ascribed to any biological product when the patient has not been studied for the true cause of his malady.

Dr. Frank A. Craig: One of the most important factors undoubtedly is the nurse. I do not think there is any individual whose influence is so important and so valuable as the nurse in getting the parents to introduce these various measures. I am sorry there were not more here tonight in order to get them enthused over this subject. I have attended several meetings of the public-health nurses in the suburbs, where we have gone to talk on the question of tuberculosis, and I have had at the same meeting various members of the city health staff who have been out there talking on the question of the diphtheria test, and they seemed extremely interested in the subject and several of them got up and told how they had had their entire classes tested out and immunized.

It is the problem you have to meet in every branch of preventive medicine. It is the question of how we are going to get the medical profession to spread it among the public. In other branches, for example, in the tuberculosis campaign, they went through the same phase, the same stage exactly. After waiting for a time for the medical profession to come forward they found this was useless, so they went directly to the public and in that way spread the information and let it come back to the medical profession through them. I judge this will have to be a campaign along similar lines.

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MAY 29

## Introductory Remarks

BY FRANK A. CRAIG, M.D., CHAIRMAN

I do not know how familiar all of you are with the question of industrial medicine, but there can be no question that during the past twenty or twenty-five years one of the outstanding facts in public-health work and medicine in general has been the change that has taken place in the relation of the physician to industry. I suppose you are all aware, for I am sure I can remember the time, when the industrial physician was merely a man connected with

a plant in case of accident. He went there to attend injured employees and that was his sole responsibility. This has gradually developed and changed until now industrial medicine is one of the large and important branches of medicine. Anyone who has tried to cover the literature in industrial medicine in the last ten or fifteen years cannot help but be impressed not only with the volume, but with the general tone and character of the articles on industrial medicine. The spirit that has imbued these men in trying to develop industrial medicine is one worthy of emulation by those in every branch of medicine. They took a branch of medicine of no practical significance and made a large and important factor out of it. Among the men who have been responsible for this development and this change is the speaker we are so fortunate in having with us tonight, one who has devoted an enormous amount of time and thought and energy to the development of industrial medicine, who always has something new and interesting to say on the subject, something that you can carry away with you. I take great pleasure in introducing to you, if that is necessary, Dr. Emory R. Hayhurst, of Columbus, Ohio.

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## The Value of Medical Service to Industry

BY EMERY R. HAYHURST, M.D., PH.D.
(By Invitation)

Importance. The practising physician at present is in the position of the "catcher" on a baseball team, since he gets the end-results of human industrial experiences. He ought to be a "baseman" or, better still, a "fielder." He ought to be projected directly into the great scheme of production and not forever played as a lifesaver.

Medical science is greatly needed in industry, for there are so many opportunities for its application. The 42,000,000 workers in the United States are said to lose from eight to ten days each on account of disability each year, which amounts to slightly less than 1,000,000 being constantly out for this reason alone. A number of establishments have shown that this eight to ten day period can be cut to as low as five days, while the National Cash Register

Company claims to have reduced it to thirteen hours in one year's experience. Sappington, in Boston, found there were 20 cases of illness to 1 of accidents in a typical industry, and that illness caused about seven times as much lost time as accidents. In England, Collis estimates that scientific medicine could save that country £150,000,000 per annum and reduce disability absence by 20,000,000 weeks.

Definition. Industrial medicine is the philosophy, art and science of medicine applied to industrial affairs (Selby).

Present Recognition. Most will agree with Selby, Emmons and others that the industrial physician has come pretty well into his own since the World War; that confidence in him has been established, and that he is being allowed to rule his own bailiwick in the better-organized plants where the real value of his services is at last recognized. Padrone systems and other commercialized schemes do exist, but such should not stand in the way of progress. They need only reform.

Purpose and Justification. (1) Humaneness. (2) Reduction of costs. (3) Increase of production. (4) Bettering of morale. Other factors are the ability of the physician to measure, alleviate and control health in industry; to reduce liability, and to see that justice is done in compensation matters.

Scope. Scientific industrial medicine covers the following:

1. *The Physiological Selection and Assignment of Workers.* This is based upon physical examinations, also upon disability experiences. Rejections may be necessary because of race, age, sex, stature, deformity, illness, communicable disease, ignorance, mental deficiency and lack of physical skill. Those rejected should always be informed, as courteously as possible, of exactly the reasons therefor, as a help to them personally, perhaps, in the securing of a proper position elsewhere. The health of executives—key men—must likewise be included in any comprehensive organization.

2. *The Hygienic and Physiological Requirements of Workers Needed to Fit Different Jobs.* At present, standards are not fully developed, but workers may be classed as: "A," able to do any kind of work; "B," healthy or normal, but limited because of stature, sex, etc., to certain kinds of work; "C," having physical or mental defects, but capable of limited employment; "D," unemployable.

3. *Hygienic Supervision Over Working Conditions.* Selby points out that this is always a compromise between ideals and necessities. The primary purpose of industry is production and not health promotion. Plant inspections should be made according to a prearranged analytical method. Comparisons with accepted standards is the only precision method. The score-card is endorsed. The scheme, in full, demands coöperative work between the production manager, engineer, chemist and physician on the technical side. These are the hub and spokes of the wheel. The foreman in the workroom is the rim of the wheel, which is in constant contact with the surface covered—the producing elements—*i. e.*, the workers themselves. All these make up the mechanism, which must have the correct environment for major production.

4. *Health Maintenance of Workers.* The physician should make definite arrangements for the care of all health complaints, the disposition of chronic disease and the special investigation of occupational diseases. Health instruction of employes means personal talks intended to clear away ignorance and to prevent exploitation. The physician likewise should guard the company against exploitation in the matter of health appliances and fads advanced by commercial interests. Communicable diseases demand practically daily watchfulness, with foremen instructed to be observant. Likewise, health officials must be quickly informed of epidemic illness of all types. Trivial illnesses, first-aid, dental prophylaxis, ocular attention of prophylactic and emergency nature, as well as the usual provisions for surgical treatment of minor injuries, should obtain. Except in isolated communities, as a rule, major surgery should go to outside hospitals. Finally, compensation approvals must pass under the physician's scrutiny.

In Ohio, over $12,000,000 per year thus changes hands from the consumer (through the employer) to the injured worker or his beneficiaries through the state fund alone.

5. *Community Matters.* It is industry's interest at all times to find the cause of human inefficiency, and often such means that the physician and his nurse must turn detectives and learn of housing conditions, food provisions, community illness, etc. He must also give medical advice on the selection of doctors, dentists, nurses, hospitals, clinics, relief and benefit organizations, and ofttimes in other matters. Much illness among industrial workers, perhaps most of it, is primarily a home, if not a community, affair. Hence industry cannot stand aloof in community health matters.

6. *Research Pursuits.* It is the duty of scientific industrial medicine to extend the boundries of medical knowledge in a field having very little other possible approaches. It seems commonplace to mention that the industrial physician must commingle with fellow-practitioners, join professional and certain technical associations and read special journals devoted to his field.

7. *Promotion of Fair Dealing in Production.* The physician stands in the van of educated persons today. He also stands in the van of those trained in the ethics of the humanities. He thus has a great moral obligation to fulfil, and in fact, occupies a unique position in the stabilizing of labor relations and the creation of loyalty and employment morale.

Examples from Industrial Hygienic Experience. (1) During the World War, a plant in Dayton, Ohio, employing over 5000 women and girls, making timers for shells, was experiencing outbreaks of apparent poisoning, possibly of enemy instigation, accompanied by much hysteria, which baffled detection for some weeks. As hot weather approached conditions became worse. Finally a careful investigation showed the phenomena to be spells of heat collapse in air-conditioned rooms where it was necessary to maintain a relative humidity of at least 60 per cent. To make certain of this, the air-conditioning apparatus was often allowed to run humidity up to 75 per cent or more, with temperatures ranging above 80° F. Correction not only stopped the "poisoning" epidemics at once, but resulted in a 10 per cent increase in general production forthwith.

2. Much "sickness" is imaginative. Many are "neurasthenically sick," especially salaried help, and at the expense of industry. This usually averages from 10 to 20 per cent of those employed. It is therefore a larger noneffective factor than tuberculosis. No lay person can handle this situation. We recall the "hard-boiled" battalion medical officer of war days whose sheer good sense, we are told, prevented as much as 25 per cent of the force from being noneffective most of the time.

3. Employment of foreigners, who often come from rural districts and are not at all accustomed to indoor industrial work, means much work for the physician on account of accidents and undue prevalence of sickness. Negroes, also, have to be watched more than whites, especially for smallpox, syphilis and tuberculosis, because their private medical care is usually much less adequate.

4. At a stove manufacturing plant, workers kept sickening who were employed at enameling in a small outside building with apparently good ventilation. However, had the whole roof been removed, *poor* ventilation would still have obtained. It took some study to ascertain why. In brief, the building was surrounded on all four sides by taller buildings only a few feet away and also had no entrance for ventilation at the ground level. It was much like a lantern set down in a box.

5. At a bunk-house and eating quarters of a construction gang at a steel-mill, mysterious poisonings occurred in the midst of the severe winter of 1917–1918. About weekly, for three or four weeks, an employee was found dead in bed and several others gravely afflicted. The first two were pronounced "ptomaine poisoning." In the third, a diagnosis of carbon monoxide poisoning was made, and made correctly. However, an investigation of the premises showed that no fires were used at night time, there were no mill buildings within several hundred yards and no gas mains in the vicinity. In short, there was no obvious source for carbon monoxide gas. The ground was covered with a foot of snow and quite frozen below that. Finally, it was noticed that at some distance from the bunk-house a little steam escaped through an opening in the snow which, a yard caretaker said, was from an old cinder dump to which nothing had been added for six months and upon which the bunk-house itself had been built months before. The dump covered several acres. Trenches dug on each side of the bunk-house ran into carbon monoxide gas at a distance of four or five feet down, some of the workmen being partially overcome while digging. Investigations showed that this gas had been passing up into the bunk-house under the kitchen portion where the warm water from sinks emptied directly under the building, keeping that part from freezing and causing it to act as a fluelike opening for the escape of pent-up gases in the whole dump area. These concentrated in the building when windows were more or less closed on the cold nights.

6. Other mysteries are often thrown to the industrial hygienist. At Lancaster, Ohio, occurred the deaths of two parents and four children one night in November, 1922. A long-distance diagnosis of carbon monoxide poisoning was made, but discountenanced by local authorities because natural gas (which does not contain carbon monoxide) was the only heat used on the premises, while

much circumstantial evidence pointed to food-poisoning. Investigation showed that in a little cottage in the outskirts of the city a small "radiant" type of gas-stove with the usual clay glowers had been installed for room-heating purposes and was being depended upon as the sole source of heat. The night had been cool. The house was new, tightly constructed, the walls moisture-bound with new plaster, the doors and windows fitting tightly. The family had experienced symptoms thought to be food-poisoning for two or three weeks previously and had reasons to fear certain enemies, but the innocent-looking little gas-stove, recently purchased and new, was never suspected. It is true, a long-headed physician had had a plumber inspect the gas connection for leakage, but they had been pronounced perfect and they were so. Experiments made in the cottage under the same conditions resulted in the death of white rats in four hours, rendered canaries unconscious and greatly affected guinea-pigs (which are known to be unusually resistent to carbon monoxide gas). The test likewise brought about an atmospheric condition in which matches would not burn (that is, there was less than 17 per cent of oxygen present) while carbon monoxide gradually accumulated in the atmosphere to over 1 per cent in the course of eight hours, in spite of the fact that the outside door, which opened directly into the death room, was opened hourly for the five investigators to enter for a few minutes and then again leave. During the experiment the air seemed fresh and invigorating at all times, because it was cool, although the eyes tended to smart. The stove itself was of improper construction and a constant generator of carbon monoxide while burning. It had no flue connection, which precaution would undoubtedly have prevented the horror which occurred.

Another instance: A bridal couple disappeared on their wedding night, presumably upon their honeymoon. They were found three days later in a partially decomposed condition in the bedroom of their newly constructed house, long since asphyxiated by carbon monoxide fumes from an innocent looking little clay glower or "radiant" gas-stove which was still burning quietly on. In our Ohio experience of the past three winters we have had 105 similar tragedies due to the room heater gas-stove in which the so-called "radiant" type or model has been mostly responsible. In all instances, stoves were not flued to the exterior. Carbon monoxide is today even more so, the greatest of modern horrors, as the *Lancet* put it as far back as 1903.

7. Industrial physicians often have to make distinctions between nuisances, which are of no real health significance, and real health hazards. For instance, a plant burning cocoanut shells to produce sponge-carbon created a peculiar pungent bluish smoke in a neighborhood, but it was impossible to establish any definite health hazard. It was a question for the courts to settle as a property damage case and not one for physician or sanitarians to dispose of.

8. Many workers have peculiarly sensitive skins, even to ordinary conditions, and cannot be employed on certain work. This is readily observed where employees have to dip their hands constantly in water. Skin specialists state that about 3 per cent of persons are so predisposed. Hence, such persons should not be employed under these exposures, and it is questionable whether we should call upon an establishment to change working conditions when not over 2 or 3 persons, out of 100 exposed, develop a skin rash, although there is no question but that such should be compensated as an occupational disease.

9. Loss of resistance, especially to constant irritants, may come at any time. A wholesale grocery company mixed its own cleansing and sanitary powders, the process being worked about once a month, but the filled cans handled perhaps daily. A man who had done this for years, without evidence of dermatitis, was later made foreman. His exposures thus became much less frequent, but he occasionally had to instruct new employees. After one such occasion a violent rash appeared on both hands, limited at the sleeve line, and shortly afterward on his face and neck. The dermatitis was persistent. After some weeks he had to give up work. After some months, with increasing suffering, he was in the hospital. Skin specialists could give him no relief. A general inflammation of the mucous membranes followed and he died within about six months of the start of his affliction. A death award for an occupational skin disease was allowed.—In his chapter on "Occupational Affections of the Skin," Dr. John T. Bowen[1] states: "As a rule, the occupational dermatoses do not occur suddenly or at the outset of exposure, but after a considerable time, sometimes several years. This acquired sensitiveness may be explained either by the accumulative action of the constant irritant, or on the theory of a gradually diminished power of resistance." We have had several similar cases in our Ohio experience.

[1] Industrial Health, by Kober and Hayhurst, p. 908.

10. Employees left by themselves often devise ludicrous if not menacing forms of health protection. Mayers, in New York State, cites the instance of laundresses wearing heavy sweaters to protect against an atmosphere surcharged with moisture and greatly overheated. Workers readily choose to breathe a dangerously gassy atmosphere, which is warm, rather than tolerate a draft for ventilation purposes, because of the greater skin comfort. Many employees believe alcoholic drinks protect against industrial poisons. Some painters adopt the starvation method for the treatment of lead-poisoning. Consumptives too often seek jobs with a gas-filled atmosphere, cement dust, weather-exposed trucking jobs, etc. Preferring a long work-spell of six to seven hours without meal-time to a slightly longer day with meal-time, is another illustration. Given a choice between better working conditions and increased pay, employees invariably choose the latter. The well man's philosophy is uttered with bravado, "today;" the sick man's, "give me relief." Neither is interested in causes and effects.

11. The tendency to call almost any affliction an occupational disease is, of course, great. One worker and a number of doctors were certain that a violent respiratory condition of several months' duration was due to breathing cyanide fumes and other gases, nominally exposed to, in a heat-treating and hardening process, to which the worker had evinced no symptoms for the previous twenty years; but the death certificate was eventually signed "carcinoma of the lungs."[1] Men who handle a piece of brass such as a door-latch or controller handle on a street car, will insist that a skin rash or an indefinable abdominal condition associated with pain and "rheumatism" is due to "brass poisoning."

12. "Safety" installations of faulty construction give a false sense of security. In a tobacco factory a large exhaust-fan over the entrance to the workroom pulled out enormous quantities of irritating tobacco fumes. Still the hundred or more employees, largely colored women, complained bitterly of the tobacco fumes within the workroom. Investigations showed that on the floor above were large drying ovens from which tobacco fumes escaped to the windows of a court between the buildings and entered the windows of the floor below, being greatly motivated by the presence of the exhaust-fan described. A case of aplastic anemia due to chronic benzol and benzine poisoning had no apparent work-place hazard to

[1] Autopsy revealed hypernephroma of the right kidney as the probable origin.

substantiate the claim because, while these substances were handled in large quantities daily, everything was under a powerful exhaust system. However, the exhaust discharged through one of the windows, whence a considerable amount of it immediately reëntered the other windows (which were open much of the time for increasing ventilation). Thus a continuous circuit was maintained, because of the negative pressure in the room itself. Here investigation showed that a strong odor of these substances was present in the working atmosphere despite the engineering provisions for removing all of the fumes at their points of origin.

Summary. Industrial physicians should lay stress on health complaints made by workers and not wait for sickness disability. Surgery, in the face of disability statistics, certainly requires much less stress than ordinary sickness. A study of the physical status and capabilities of individual workers and constant plant examinations for health hazards are the important things.

The small plant presents a serious problem, since it cannot finance a health service by itself. McCord states that over 99 per cent of the manufacturing establishments in the country are small ones, that is, employing less than 500 workers, and over 60 per cent of all workers are in these smaller plants. Probably less than 1,000,000 workers are now included in industrial medical services in the country and a large part of these are only under an emergency supervision for accidents.

Lay supervision cannot be considered effective in any sense, because of a number of factors which lay persons fail to comprehend, such as peculiarities of age, sex, physical stamina, physical defects, mental attitudes, incipient disease, convalescence from disease, malingering, etc.

The medical man should sit in on all questions of heating, lighting, ventilation, the using of poisons, compensation policies, strikes and, in fact, practically all instances of human unproductiveness. No expert in industrial production can show better results than the intelligent "M.D." All safety appliances should be approved by one who has a "biological mind."

We note that McCord, Selby, Emmons and others have shown how to set up industrial medical services for small plants, and their various writings should be consulted.

Where medical services cost no more than $2.00 or $3.00 per capita per year the adequacy may be considered a "blind" in most

instances; $10.00 per year is palliative; $25.00 per year will usually provide a minimum but complete industrial medical service. There is no reason, so far as I can see, why the workers should not be expected to stand a share of this. Only preventative and emergency measures should be provided; curative measures belong to private arrangements.

Price states that "the most dangerously unguarded machinery today is that of factory inspection for health purposes." Under our present system of lay personnel, usually entirely uninformed in matters of technical hygiene, factory inspection can easily be shown to be "dangerous." Worse still, small plants are left practically unsupervised by any kind of sanitary inspection worth the name.

The field for extension is, therefore, unlimited. The physician has a world before him. It is to be noted that people are becoming more and more interested in certain industrial-domestic matters, particularly poisons, as evidenced by the recent agitation in regard to lead-poisoning from the use of a new gasoline having an "anti-knock" property; or, more in particular, the constantly recurring deaths from gas-poisoning which are slowly coming to be looked upon as someone else's responsibility, many times, than the ignorant victim. We have also the American Medical Association's campaign for limiting the promiscuous sale of lye. All of these things are slowly leading to a Federal supervision of interstate traffic in poisons and to regulations similar to the food and drug laws.

Finally, as this field expands, opportunity for consulting services in industrial disease and accidents is at hand. I know of no other field which, to the physician with a detective-like instinct for discovering ultimate causes of disabilities, has a stronger fascination than this one of industrial health.

## DISCUSSION

Dr. H. F. Smyth: The subject of Dr. Hayhurst's talk is one in which I have been intensely interested for some time and I can only endorse heartily all of his points. I would like to emphasize by illustration several of his points from personal experience and observation. I have in my work had an opportunity of visiting periodically a number of industrial plants and seeing them grow up and develop in their operations and in improved methods and improvements of the health hazards of these plants.

I have seen several plants adopt medical service and I have never known a plant in my personal experience that once it has adopted medical service that did not in a comparatively short time become absolutely sold to the idea. Where the plant having medical service dropped it this is usually due to a change of management, the new management has not been sold to the idea. Two plants I have particularly in mind near Philadelphia; one plant manufacturing anilin and anilin products, a plant where if you walked through it you could pick out cases of anilin poisoning, see it on the faces. As a result of our recommendation they took on a full-time physician. The production manager did not think much of the idea, but during the war they usually did what they were told in these lines. Visiting the plant some two years later, while carrying out some special work, the production manager said to me: "You know I did not think much of this thing of having a doctor when it was first brought to me. I am absolutely sold to it now; I would not be without him."

About the time I first took up this work, in 1915, I asked for the privilege of taking my students through a large industrial plant in the Philadelphia district. The reply was: "We will be glad to have you come, but we have just begun to employ the physician since the first of the year and I do not know that we have much to show you." That is just the kind of a place I wanted to go. They employed a physician there, but did not have enough work for him to do, so smaller plants in the neighborhood contracted to use part of his time. In a very few years he had to give up work in smaller plants and devote all the time to the one. In a few years he had quite a staff of assistants and nurses under him and one of the other plants had a physician and nurses, showing how absolutely sold they were.

Emphasizing the point Dr. Hayhurst made at the last, speaking of cost of medical service, if you pay a little you will get your money's worth, but if you pay more it will be a profitable investment.

Now as to the influence of the true industrial physician, not just a plant doctor: The influence on morals no one can help but appreciate after he spends any time in the plants where full-time industrial physicians are employed and see the reaction between the doctor and the men who come into his dispensary and the men he sees as you go through the plant with him. It is certainly very interesting and stimulating to see how such a man can get a grip on these employees and acting as a liaison officer, as it were, between the employer and the employee, making for better spirit and better morale in the whole plant. There is no question of his ability to do this.

Dr. Hayhurst mentioned the opportunity that the industrial physicians have at times for investigating special conditions. This was very well illustrated in a preliminary report that he and I had the privilege of hearing the first of this week before the meeting of the Industrial Physicians and Surgeons. An industrial surgeon's attention was attracted to a case of tetanus developing from a wound, the nature of which would not lead you to dread tetanus in any way. As a result of that he started an investigation through his connection with other industrial physicians, sending out a questionnaire and analyzing the results. His report when completed will

be available not only to industrial physicians but to surgeons and will develop bacteriological facts in relation to tetanus that were not clearly appreciated before.

Miss D. E. Wiesner: Dr. Hayhurst spoke of tuberculosis as being very prevalent among industrial workers because of hazardous occupations. Do you mean just because they are placed in hazardous positions, or would you attach more significance to tuberculosis in industry? I was wondering whether an industrial physician can be proficient in more than one type of plant, such as metal industry, textile industry or food products plants. Could he serve all three with the same competence?

Dr. Hayhurst (closing): Philadelphia is the first city to my knowledge to make a survey of its industrial medical services. Several cities have made attempts at industrial health surveys—Cleveland, Chicago, New York—but they have been of limited character. Buffalo is now, I understand, undertaking something along this line; also Boston. Nothing has approached the thoroughness with which your tuberculosis organization is proceeding here.

The small plant situation can be solved. I would refer to the work of Dr. A. B. Emmons, 2d, who is with the Harvard group at Boston, and to that of Dr. C. P. McCord, who is with the University of Cincinnati. Dr. McCord is conducting an independent "industrial conservancy laboratory." Both of these men have the wholesome scientific spirit and, in spite of the business of their daily programs, succeed in getting out one or two original researches each year. I question whether small-plant work should be undertaken by physicians who devote the balance of their time to general practice, except perhaps in a purely advisory capacity. Part-time work is probably better in connection with a large plant, for I believe the physician should always avoid the liability of fixed routine (except for a year or so for experience) and also keep an anchor to leeward in case of sudden severance of his income relations. But the diversity of experience, also the lessened importance of tenure of office with any one small plant, may permit a physician to devote full-time, safely, to the general subject of small plants. The loss of one or two connections here and there will not upset him, while his work will likely be generalized enough. He should organize a group of as many small plants as he and a competent staff can supervise with justice to the situation. The medical work should be done at each plant, not elsewhere—as at a central dispensary, which cuts off plant contacts too much. As the health and well-being of workers is a production affair vitally related to plant conditions, it should be taken care of as much as possible on the grounds of the plant. The balance of the plant is usually run on the same principles, especially personnel affairs. Also, Emmons found that it was not well to assemble employees from different plants in a common waiting-room. They tend to compare notes, which leads to dissatisfaction.

Any physician undertaking this sort of work should acquaint himself at once with the health standards commonly accepted for the various

hazardous conditions of work, for physical examinations, for the set-up of staff organizations, dispensary equipment, etc. The usual textbooks in the field are sufficient guides for the usual procedure. Beginnning with optional or voluntary physical examinations in order to establish confidence, and including the plant officials, one should soon be able to work up a most worth-while service, appreciated by all concerned. The industrial physician should not be hampered by being placed under the legal department or engineer or any other technical personnel of the organization than that of the production manager or the president himself. His problems are usually much more intricate than those of the technician and he needs latitude.

The services which have been started in the manner indicated have continued to grow, are commercially successful, ethically founded and fill a great need. Furthermore the incentive to effort is retained. There is no doubt but that they will soon multiply. A few persons interested intensively in any fundamentally economic program are certain to accomplish greater results than many who have only a languid interest.

It has been fifteen years since Dr. Ludvig Hektoen, then a member of the Illinois Occupational Disease Commission, suggested that I enter this field of work. I had just completed my hospital training at Cook County in Chicago, where I had run into many instances of occupational diseases and had taken occasion to show some cases of lead poisoning in factory girls before the Chicago Medical Society in 1909. Dr. Alice Hamilton was the director of the Illinois Survey. I have played the subject as a "hobby" ever since, first with private practice and research, then in the conduct of the Ohio Survey of Occupational Diseases, and for the last ten years with teaching, state work, dispensary practice and consulting work. Some ten or twelve years spent in factory work during summer vacations, when fourteen to twenty-five years of age, have stood me well in hand. One summer (1904), between college and medical school, I helped to "boss a gang" of children on a truck farm.

Industrial physicians can be stimulated in their research work, I think, by insisting that they keep in touch with the educational institutions at hand—not only with the medical college staff, but with the engineers, chemists, sociologists and others. Admit them to your university or faculty clubs. I think, too, that you professors should go out of your way somewhat to get in touch with industrial physicians and surgeons, and get them to tell you of their problems and to permit you to make contacts which they greatly need and would appreciate. Otherwise the industrial physician, whether part-time or full-time, easily falls into the rut of routine and soon imagines he is all-sufficient in his little world and ceases to grow. I think routine does this for anyone. Usually, if he can once be prevailed upon to do a little research or case reporting and publish something, he is started on the right road.

The question of tuberculosis in industry, which Miss Weisner raises, is a very broad one. I expect to say something about it at the Minneapolis meeting of the National Tuberculosis Association in a few weeks. Our best statistical and actuarial experience, both in Great Britain and this country, shows that there is something inherent in industry that incites

tuberculosis. I suppose the mere fact of putting youths into indoor jobs at long hours is the basic reason. Such is contrary to Nature's idea. Twelve years ago we investigated the industries of Ohio and reported upon the same in 1915. We were surprised at that time to find that the census figures obtained from Washington showed the highest death-rates from tuberculosis occurred among telephone girls. It was hard to understand why that calling should be productive of such results. About that time the telephone companies began to inaugurate physical examination for new employees and, I think, solved the question quite definitely: the more delicate girls, many on the verge of consumption when employed, were gravitating toward the "easy indoor job." Such is undoubtedly true of many callings. Clerks and stenographers are another example whose rates exceed those in factories and shops, as a rule. The negro, foreigners and country people entering industrial life appear to be without as much resistance as city-bred persons. The ignorant are most likely to be placed in the most health-hazardous jobs in a plant. We have, of course, certain industries in which tuberculosis is ten times as high as the average for "all males." Dr. Winslow and Dr. Hoffman cite the grinding and marble-cutting processes, respectively, as examples of this. In Ohio, in 1913, we published a list of trades and callings in relation to tuberculosis morbidity statistics, based on the census reports, copies of which may still be obtained by addressing the present State Department of Health at Columbus. Necessarily changes have taken place in these rates in the more recent years.

The physician who handles the small-plant organization is usually qualified to take in quite diversified types of industries. While Dr. Emmons limits his to mercantile establishments, Dr. McCord includes widely different industries. A chief difficulty is the securing of properly trained personnel for different phases of the work, since so much environmental hygiene has to be taken into consideration. At all odds, none is better equipped for accomplishing the work than the physician who is specializing in the subject. Under lay hands it is getting nowhere and much botch work results. This is because hygiene, diagnosis and medical treatment are fully as important as engineering, sanitation, sociology and "management" in the solutions required.

Mr. Harvey Dee Brown (By invitation): I want to express my appreciation of this very concrete and clear exposition of industrial medicine. I am not competent to say anything specifically about industrial medicine, but it occurred to me that you might be interested in knowing how extensive industrial service is in Philadelphia. With the Association of Industrial Medicine, the Health Council made a survey to determine the extent of industrial service in the city. As I recall the figures, there are some 6500 industrial plants in Philadelphia. Of that number 4500 are small plants having from 2 to 25 employees. There are 1882 plants that have over 25 employees. Dividing these into two groups, as we did, those who have 300 employees or more make a group of large plants of 193 in Philadelphia. Of the 193 large plants here there are 42 which have what we classify as

"complete" medical service and 34 have what we classify as "incomplete" medical service. When we got our reports in we found the service differed so widely we had to make some classification, and for the purpose of stating the facts we decided every plant which had physician, nurse and dispensary would be classed as "complete" medical service. Where they had two of these elements we called it "incomplete" medical service. We put in a group of "emergency" service, those having a first-aid cabinet only. There are 76 plants out of 193 having "complete" or "incomplete" medical service in Philadelphia. There are 52 large plants which give no attention to health. Some 65 others have what we call "emergency" service.

Of the smaller plants we did not get reports from all, but we did from about 850 of them and found that of these plants very few had anything like "complete" medical service. I think it was 4. In these plants the service was connected with some large plant, a sort of satellite affair. About 30 had "incomplete" medical service. Some 300 had "emergency" service, that is a first-aid cabinet.

I do not know how that survey would compare with other cities. It shows something is being done here. I am interested to know if there has been a similar inventory made of industrial service in other cities.

I was much impressed by the fact mentioned by Dr. Hayhurst that the small plant needs the help. The larger plant with 300 or more employees, if they want to establish medical service can do it. They can have physician and nurses. What is the small plant going to do? They cannot get part-time of a nurse and if they are going to hire medical service it is going to be expensive. The Health Council is planning as soon as possible to organize a unit of five or six small plants, having enough employees to justify us employing one or more nurses and part time of a physician, so as to supply these plants with the medical and nursing service they need at a *pro rata* cost.

The Philadelphia Health Council is a voluntary organization. We are not engaging in industrial health work for any other purpose than that of promoting public health. We would by this means furnish plants with full service at practically a cost figure and carry the service on for a year or two with the idea that after that a committee of the plants could keep it going. Possibly this may help meet the situation in small plants.

# PROCEEDINGS

OF THE

# SECTION ON MEDICAL HISTORY

## GALEN'S DISCOVERY AND PROMULGATION OF THE FUNCTION OF THE RECURRENT LARYNGEAL NERVE*

By JOSEPH WALSH, M.D.

We have several portraits of Galen, none of absolute authenticity. On a manuscript edition of Dioscorides, from about 500 A.D., is an alleged portrait as an old man, whether or not an actual representation we do not know, yet there is no impossibility that it may have come down on succeeding manuscripts.

On a medal struck during the reign of Commodus is a man representing Pergamum. Fabretti and Bonarotti assert that this and the portrait of the old man called Galen on the aforesaid manuscript are the same at different ages. The marble bust in the hall of the College of Physicians, presented by Dr. Richard H. Harte in 1912, appears to have been made from this medal. It is the portrait to which I am personally most attached.

Fig. 1 shows four portraits: On the top row the seated old man from the manuscript of Dioscorides, and the full figure on the Medal of Commodus. This medal shows two men holding statuettes evidently representing Pergamum and Ephesus, since the two cities are designated below. The representative of Pergamum is a man about the age of fifty to sixty with the mantle of

* Read March 24, 1925.

Aesculapius about him, the statuette of the god in his right hand and the baton in the left. He has a sort of turban on his head which was usually put on images of physicians to indicate their calling.

FIG. 1.—Four portraits of Galen.

The other figure, representing Ephesus, has not been identified. He holds in his right hand a statuette of Diana and in his left a spear of Artemis Agrotera (the huntress).

On the second row a typical Roman of the first century, when clean-shaven faces were in vogue. Beards came in again with Hadrian, and, following the custom of philosophers and physicians, it is likely Galen wore one. I have no reason to believe it a portrait of the master.

My own impression would be a medium height, homely, intellectual-looking man with a definite eastern cast of countenance, aquiline nose, prominent chin; not particularly prepossessing either in appearance or address. He was convincing in language on account of his broad knowledge and sincerity, yet so overready to argue and contradict as often to arouse an antagonism preventing conviction. Since he was, however, one of the most brilliantly educated and most industrious scientific workers, thinkers and writers who ever lived, with a quick temper which made him one of the most belligerent talkers, it is safe to put all this in his physiognomy. The fourth portrait would not be unfavorable to this description. I do not know its source, though it is sometimes seen parading over his name.

Previous to his time it was the popular idea that the center of intelligence and thought was located in the chest, and the brain was only for the purpose of cooling the blood. The argument of Diogenes of Babylon still prevailed, that we speak with the larynx, and the impulse to the movement of the vocal cords being from the lungs, thought must be some place in the chest and probably in the heart. Galen's discovery showing the connection of the brain with the vocal cords, and their failure to act when the recurrent laryngeal nerve was divided, settled the question for all time.

In order to understand some of the side features accompanying his demonstration of this discovery to the Romans, and their skepticism, a short review of his career is necessary.

He was born in Pergamum, Asia Minor, 130 A.D., and given a very careful training in the classics, philosophy and medicine. His native city was one of a galaxy, comprising Smyrna, Ephesus, Rhodes, Cos and Miletus, which represented the highest in art and education in the world. Their importance may be seen from the fact that Cicero, Caesar, Brutus and Cassius studied their oratory at Rhodes. And Galen justifiably assures us that the temple of Aesculapius at Pergamum, where he studied medicine, was the most illustrious to this god in the world, and was as well known as

the temple of Diana at Ephesus or of Apollo at Delphi (xiii, 271[1]). This is confirmed by a letter of Marcus Aurelius to Fronto, about

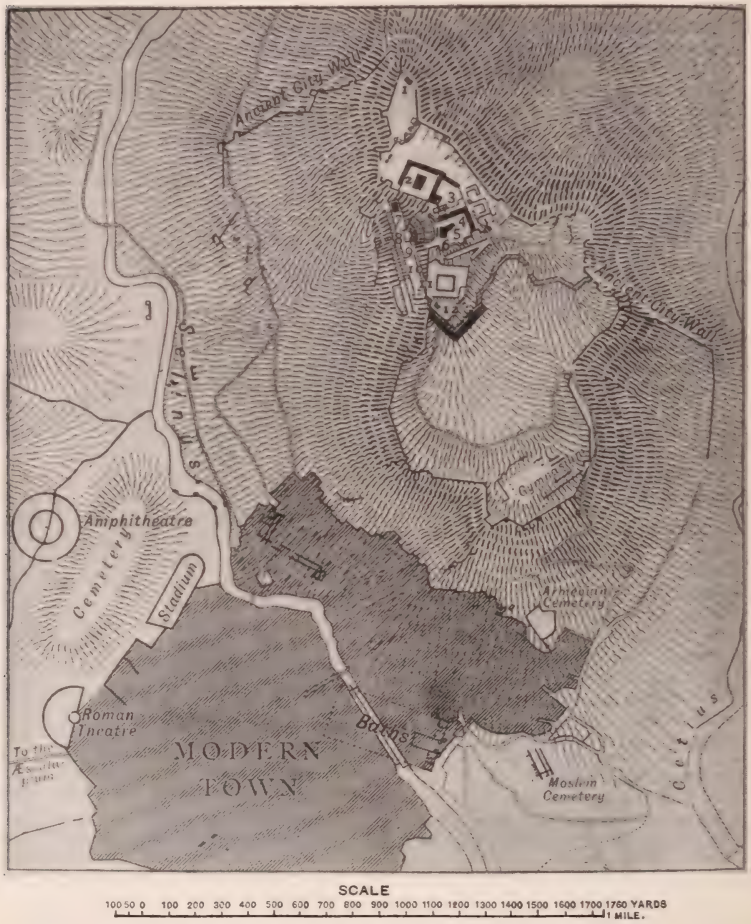



FIG. 2.—Plan of the present Pergamum, by Dr. Karl Humann, from Murray's *Handbook of Asia Minor*. Only the merest ruins exist of the ancient buildings in the town and on the acropolis. Galen was surgeon to the Amphitheater and medical director of the Gladiatorial Training School. The cemetery is modern. The Temple of Aesculapius, at which he spent four years in the study of medicine, was about 2000 feet from the Roman theater. 1. Temple of Julia. 2. Temple of Rome and Augustus. 3. Library. 4. Stoae. 5. Byzantine Church. 6. Temple of Athene. 7. Ionic Temple. 8. Theater. 9. Church. 10. Great Terrace. 11. Altar of Zeus. 12. Temple of Dionysus.

[1] The references in parentheses are to the volume and page of Kuhn's edition of "Galen."

142, praying for every good fortune on his birthday, in which he informs him: "I climb first the citadel of the god of Pergamum and beseech Aesculapius to protect your health; I pass on to Athens and clasping Minerva by the knees, etc." According to Friedländer,[1] in Byzantine times it was considered one of the wonders of the world.

The city was situated half on a beautiful plain and half on the hill ascending to the acropolis, as the accompanying plan shows. In the city proper was the amphitheater, where Galen at the age of twenty-nine became medical director of the training school and

Fig. 3.

One Section of the Market Place (the Directors' Conference Room) was probably built by Galen's Father, who was an Architect. Heliogravure Lemercier. From "Pergame," Pontremoli et Collignon, Paris, 1900.

surgeon to the gladiators. This amphitheater was about the size of a Philadelphia city block, being 450 feet in diameter. A small tributary of the Selinus ran through it, which when dammed gave opportunity for nautical sports.

On the acropolis, 600 feet above the plain, were situated most of the official buildings, among others a temple to Augustus, to Athene, and an altar to Jupiter, which was one of the most famous in the ancient world; in fact, the recent excavation of this altar and the temples about it has given us new ideas relative to antique art and the possession of these sculptures has raised the Berlin Gallery

[1] Roman Life and Manners under the Early Empire, trans. by Magnus, London, vol. ii, p. 325.

to a rank near the Louvre. On the acropolis, also, were the schools, the market place and a beautiful theater overlooking the plain. Mahaffy says of Pergamum: "We do not know of any Hellenistic city, except perhaps Rhodes, where life was more refined, morals better or learning more respected." And Pliny calls it "the most celebrated town in Asia Minor."

At the temple medical school, located just outside the town near a mineral spring of great renown, he spent four years; but not satisfied he continued his studies in Smyrna for two more, and then with the wonders of the school of Alexandria in his mind he betook himself to Egypt and remained five years, broadening himself in mathematics, astronomy, philology, philosophy and medicine, and imbibing a love for anatomy and physiology which never left him.

On his return to his native city his medical knowledge was early recognized and he was appointed to the highest position of the city, namely, surgeon to the gladiatorial amphitheater. Here he began the anatomical and physiological research on dead and living animals for which he is entitled "The Father of Experimental Physiology."

The thoroughness of his dissections is evident when we learn that to an already well-described muscular anatomy he added the superior palpebral, buccinator, platysma myoides, the palmaris, plantaris and the interossei of the hands and feet, and in every other realm of anatomy added as much. As a student in Smyrna he had become interested in the movement of the chest in respiration, and continuing this work he unfolded for us the complete story as to the influence of the diaphragm and the intercostal muscles. It was he who discovered the decussation of the fibers of the intercostals and its significance. In this study he cut the phrenic nerve and watched the action of the intercostal muscles; then, by a difficult operation on another animal, cut the intercostal nerves at their exit from the spinal canal and watched the action of the diaphragm alone. It was while dividing the different nerves in the vicinity of the lungs, to learn their influence on respiration, that he accidentally discovered the function of the recurrent laryngeal.

The manner of discovery is evident. The pig was tied on the table without an anesthetic and only kept intermittently from squealing by the hardy hands of a slave. The recurrent laryngeal was cut and in a dramatic fashion the squealing stopped instantly.

Further experimentation showed that section of it not only prevented the pig from squealing, the dog from barking, but all other animals from emitting their peculiar cry.

As stated, this discovery established for all time that the brain is the organ of thought, and represented one of the most important additions to anatomy and physiology, being probably as great as the discovery of the circulation of the blood. If he never did anything but this he would deserve a place beside Erasistratus, Herophilus, Vesalius, Harvey and Virchow.

FIG. 4.—Galen in the amphitheater of Pergamum, treating a gladiator wounded in the act of playing the part of the retiarius, as indicated by the net and trident. Illustration from about 1870 by Jan Verhas (1834–1896), the well-known Belgian genre-painter, whose most popular work, the "School Feast" is in the Brussels Gallery. The illustration is evidently made with the idea of showing as much of the life of the amphitheater as possible; hence we see Galen treating the gladiator in a room associated with the animals' cage, though it is very likely there was a special surgical operating-room, and with Galen's insistence on cleanliness he would not be wearing the toga. Figuier *Vies des Savants*, Hachette et Cie, Paris, 1870.

In his physiological experiments he mentions (xiv, 627) most frequently pigs, goats and sheep, both because they were handiest and because he recognized the physiological similarity of the pig to man; in his anatomical researches he employed apes, for he says to his students (xiii, 604): "After examining carefully the position and size of nerves and tendons in apes, you will recognize

them easily in the human body; but without this, your surgical work is vain." He also tells us that he dissected horses, asses, mules, cows (ii, 352), lynxes, stags (iii, 844), bears, weasels, mice, serpents, many kinds of fish and birds (ii, 548), and at least once in Rome an elephant (ii, 619). He says he never dissected ants, gnats or fleas (ii, 237). Unlike some others, he never dissected human bodies either of enemies killed in war (ii, 385), or of dead, exposed children (ii, 386).

With the difficulty of housing in a city dwelling the large animals employed, it is interesting to speculate on where he did this wonderful series of physiological experiments. Three possibilities occur to us: The stable of his own farmhouse on the road to the seaport Elaea; an apartment associated with the quarters for animals destined for sacrifice within the precincts of the temple of Aesculapius, or for the animals destined for the arena connected with the amphitheater. After consideration, I believe he worked in all three, assisted by his slaves on the farm and by students and priests or gladiators in the other two places, to whom he took pleasure in demonstrating his new findings or anatomical facts previously unknown to them.

Though Galen's father was an architect by profession and one of the most intellectual and opulent citizens of Pergamum, he owned a farm in the country which he apparently worked as a gentleman farmer, and in addition to deriving the ordinary products of agriculture, carried out on it a number of experiments in connection with the growth of plants and the aging of wine (xiv, 17). It is evident, therefore, our physiologist derived his investigative turn of mind by heredity, and in his early student days it is not unlikely that when animals were butchered on the farm the father took pleasure in studying with him the comparative anatomy.

Galen tells us his mother was mean, nagging and quick-tempered, and there is question that this farm was the father's occasional refuge from the wife, whom the son is forced to compare with Xantippe. He describes the farmhouse, and I have introduced a drawing made from his description, for it is probable that this retreat, purchased to afford escape from an impossible woman, represents the mother of physiological laboratories.

The Parthian War breaking out and interfering with his research in Asia Minor, he hastily packed up and went to Rome at the age of

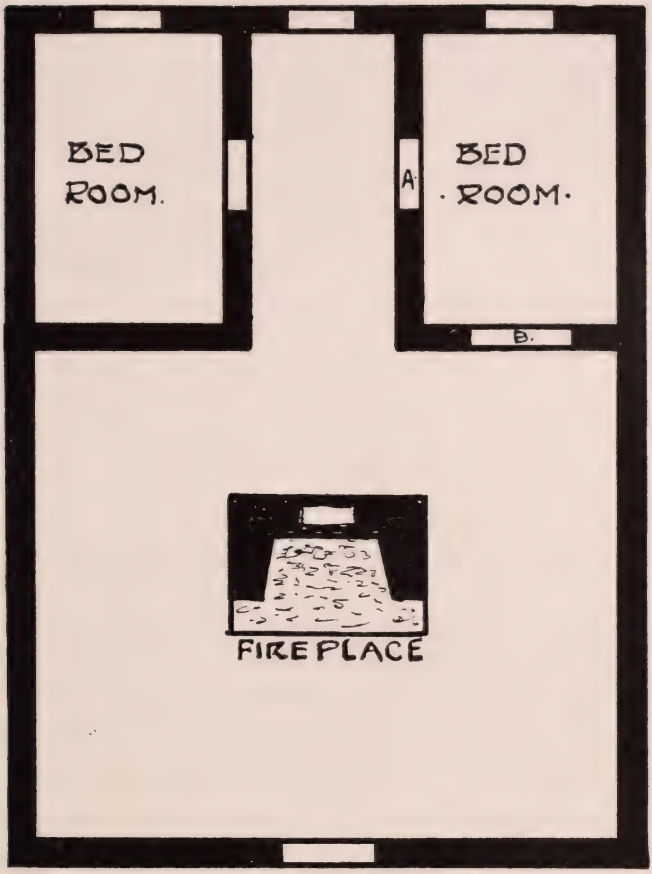



FIG. 5.—Dwelling house on farm outside of Pergamum owned and operated by Galen's father, for purposes of agriculture and carrying on experiments with almonds, peas, beans and lentils, and experiments in connection with the rapid aging of wine. The house (drawn by Mr. A. Britt) is described (xiv, 17) by the son in order to show where the wine was stored. It was a one-story, large living-room with a fireplace in the center; attached to the back was a lean-to extension with two bedrooms. Around the walls of the living-room were cabinets and receptacles for household necessities. *A*, represents the door of a bedroom; *B*, the opening into an attic space (the storage place of the wine) above the bedroom, so that the wine would be kept warm by the heat from the fireplace in the living-room. A stable is mentioned in general terms as not far distant from the house, and from his writings apparently housed one or several horses, donkeys and possibly mules, a number of goats, sheep, pigs and cows (v, 41), and the farm wagons and implements. Here in the shade of the house or the nearby trees, enjoying the thyme-scented breeze (xiv, 22), far from the disturbing voice of his nagging wife, sat the sire meditating on a new architectural plan, on the agricultural experiments he delighted in, or day-dreaming on the prowess of the brilliant son, of whom he was so proud. It was on this farm the kiddie, watched over by slaves, climbed the hayricks, in front of this fireplace played as he details (ii, 17) with the inflated pigs' bladders, exhorting them, as he pushed them toward the grate, to grow bigger and bigger, which they did on account of the heat; on this farm the stripling rode and planted and mowed, and in this mother of physiological laboratories the medical student and physician performed at least some of the vivisection investigations on pigs and goats which give him his title of Father of Experimental Physiology.

thirty-three. Galen's eleven years' study of medicine had made of him a modern regular. There were at the time a number of medical sects, the four principal being the Dogmatist, Empiric, Pneumatist and Methodist. The last had been founded in Rome two hundred years before by Asclepiades, friend and physician to Cicero, and enrolled under its banner were most of the Roman physicians. Methodism was an offshoot of the Epicurean-Lucretian philosophy in vogue at the time of Caesar. It denied an overruling Providence and contended that all things existed by chance. It asserted that the body was a fortuitous coming together of atoms, and that there was little, in fact almost no relationship between its different parts. As a consequence the study of anatomy and physiology was futile. Between the atoms making up the body were invisible pores, and disease depended on whether these pores were too tight or too loose. All diseases being classified under these two heads, it was possible to learn the whole art of medicine in six months.

Galen was one of the most pious of pagans, surpassing in this regard everyone, except possibly Marcus Aurelius; in fact, the pair of them represent the best-known pagan saints. To deny Providence, therefore, was bad enough; but to add that his beloved science at which he spent eleven years, could be learned in six months, so enraged him that from the time he met his first Methodist in Alexandria till he died, forty-seven years later, he never stopped railing against them. Unnecessary to say, he made himself immediately unpopular in Rome, where their number was greatest.

During his first six or seven months in the capital, while gaining the enmity of the physicians, he became acquainted with a number of philosophers, especially platonists and peripatetics, who were interested in his anatomical and physiological investigations, and when the physicians disdained, they took him up.

One of these philosophers was Eudemus, whom Galen cured of quartan fever. Through him he met Boethius, a peripatetic, who had shortly before been consul, and who became Galen's greatest stimulator. Insisting on the Pergamite demonstrating this wonderful discovery, Boethius said he would supply the animals necessary, and had at hand both goats and swine, and if monkeys were required he would procure them also. Consenting, our physiologist stated that since all larger animals show a similar larynx and utter not

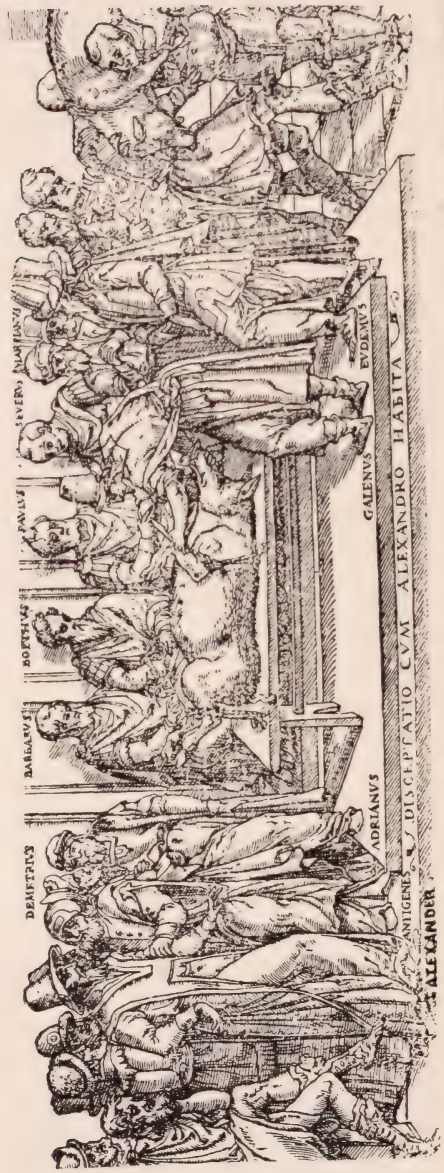
dissimilar sounds, monkeys would be superfluous; the demonstration was, therefore, on a pig.

Many of his subsequent lectures were in the Temple of Peace; but it would seem this first was in a hall hired for the purpose by the Consular. Quite a number of philosophers, especially peripatetics and platonists, came on the invitation of Boethius, who had personally advertised it widely, among others, his own assistant Adrian, Demetrius Alexandreus and the eminent Alexander Damascenus. Galen took particular pride in having the last as auditor, and when he mentions (ii, 218; xiv, 628) this address insists on his presence.

Galen's medical rivals had discussed the subject freely with the philosophers and stated their opinion in regard to some of the new ideas he was to present (xiv, 626). One of these was Alexander Damascenus, and they apparently persuaded him the Pergamite was describing things in anatomy which did not exist, or at least drawing conclusions from them in relation to physiology which were not justified. Alexander, therefore, as well as other philosophers, accepted the invitation not only in a skeptical frame of mind, but determined to prove Galen wrong. A certain number of physicians even went to heckle him, because in the meantime he was practising actively, talking freely and expressing on every occasion his low opinion of them.

On the case of Eudemus he had offended Martianus, author of a work on anatomy which was standard for more than thirty years, and Antigenes, apparently one of the best-educated Dogmatists in the capital. Between this case and his demonstration he was called to visit the well-known rhetorician Diomedes on the Sandalarium. This was the street of bookstores and publishers and a common meeting place of physicians. The most eminent of the court medical men were in attendance and had diagnosed a simple ailment which would be well in several days. Galen, apparently with his usual ostentation, diagnosed a chronic condition which would be of long duration (xiv, 625), and though it proved true he had added other enemies.

Before beginning, our lecturer gave a little explanation of what he was about to demonstrate, namely, the larynx, its muscles and the attached nerves, which being cut, the animal is rendered mute. though neither life nor action is interfered with. "I did this,"




(*From Junta Edition of Galen*, 1586.)

FIG. 6.—Galen's demonstration of the recurrent laryngeal nerve. Antigenes, a dogmatist, and Martianus, a pneumatist, were two of Rome's most eminent physicians; the others who are named were among the most eminent of the capital's philosophers. To Boethius we owe a special debt of gratitude.

says Galen, "not so much to relieve my embarrassment as to let Alexander know what to expect." When he had finished the crowd looked at the Damascene. On this cue he arose, and though those near urged him not to begin a controversy, since they were anxious to see the demonstration, he, taking advantage of the regard which all had for him since most of them (among others Boethius) had been his pupils, made quite a little speech and wound up with the statement: "Even if we are shown that section of these nerves in animals renders them mute, it is not necessary to believe it true of human beings." On hearing this Galen rose, and putting aside the dissecting instruments said he had erred, and he would not have come if he thought he was to talk to such unteachable skeptics, and without more ado he departed.

Immediately the audience turning on Alexander, upbraided him for his interference, and even Adrian and Demetrius, who were ordinarily conciliatory in speech, used violent language. Likewise, when others in the capital interested in scientific investigation, especially the noble and illustrious Severus, Paulus and Barbarus[7] heard of it, they were loud in their denunciation and requested the young physiologist to appear again in the absence of the dissenters, since even without them the audience would represent the most eminent in medicine and philosophy in Rome.

By this time Galen's ire was up, and in his own words he decided (xiv, 626) to follow Homer's suggestion, which is almost literally translated in Polonius' advice to Laertes:

> "Beware
> Of entrance to a quarrel; but, being in,
> Bear it that the opposer may beware of thee."

This time the demonstration was entirely successful, and the audience was so interested it returned several days, while he showed on the living animal the action of the intercostal muscles and diaphragm and the influence of each on respiration. He pointed out, as a discovery of his own, the obliquity of the former and the decussation of the internal and external fibers. He cut in succession the intercostal and phrenic nerves to show their particular action (ii, 660, 677). He further demonstrated the larynx, the vocal

[1] The son of the first married the daughter of Marcus Aurelius, the second was the prefect (practically mayor) of the city, the third was the uncle of the co-Emperor Lucius Verus.

cords, the cartilages and muscles connected with them, and finally, the innervation, and followed the nerves around the arch of the aorta and subclavian artery to their junction with the pneumogastric (iv, 278). Severing them on a squealing living animal he dramatically proved the loss of the voice.

All present were convinced, and Boethius was so fascinated he requested a complete account and insisted on sending his stenographer so that Galen might have as little trouble as possible, for though the Pergamite almost surely had a slave secretary, it is possible he did not write shorthand. On completion of the dictation the Consular, at his own expense, had the books published and distributed broadcast.

The author's little account of this demonstration, dictated for Boethius, as well as his book on the voice, composed later, has been lost; but he goes into the subject so in detail in his work on the "Use of the Parts," and this is written so like a lecture, that I have no doubt we have here not only what he said, but the manner in which he said it. His description (iii, 409; iv, 465) of the muscles participating in the movement of the chest in respiration is too long to detail, hence we will limit ourselves to an abridgement of his demonstration of the larynx, which probably took up one of the several days the audience came to hear him.

It must be remembered that neither he nor his contemporaries had any idea of the contractility of muscle fiber. When it was discovered I have been unable to learn, but fourteen centuries later we know that Vesalius practically understood it. It was only about 1740, however, that Haller began to differentiate in any accurate manner between sensibility, irritability, elasticity and contractility. Galen thought nerve fibers divided up in the body of the muscle for some unknown reason, and came together again in the tendon, and it was the tendon, or rather the nerve in the tendon, which contracted, and the apparent contraction of the body of the muscle was only the slack thus produced.

Believing, therefore, a certain amount of actual pulling power was exercised by the nerve, it was necessary that it enter the muscle in the direction of pull. On account of the position of the vocal-cord muscles, the nerve must come from below, and he goes into a long explanation as to the ingenuity of the Creator in accomplishing this.

"If," he says, "the heart was the origin of the nerves, as certain people thought who knew nothing of anatomy" (he is particularly hitting Aristotle), "it would be able to move the muscles of the vocal cords by sending the nerves direct from the heart to them, though a parallel difficulty would arise in connection with the muscles in the neck, which have their heads above.

"With the brain the origin of the nerves, it is necessary to understand the action of a pulley as employed by builders or by the orthopedists in the glossocome. Surprising as it may seem, the pulley was made use of by nature previous to its employment in the arts, in order to communicate the proper action to the muscles of the larynx."

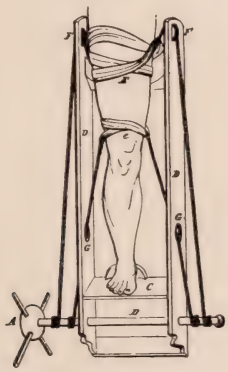


Fig. 7.—Glossocome of Galen. (*From Oeuvres D'Oribase, vol.* 4, *Paris*, 1862.)

He describes the descent of the pneumogastric, the branches it gives off, and eventually the recurrent laryngeal. On account of the fact that if this nerve were sent directly to the laryngeal muscles it would act improperly, the Creator was obliged to make it descend into the thorax until it met a transverse post which could act as a pulley. The only object it met high in the thorax was the clavicle, but to use this would allow the nerves to come so close to the skin as to be exposed to every kind of injury. As a consequence He was obliged to conduct the two nerves onward until on the left the aorta was reached and on the right the subclavian artery—these being sufficiently transverse and sufficiently solid, were employed.

"On account of the fact that some of you may not understand the mechanism of the pulley, I will draw an illustration from a more common object, namely, the spina in the Circus Maximus. As the runners in the double course wind around the spina so the recurrent laryngeal winds around the aorta and the subclavian artery.

"I want you to realize that what I am describing was discovered by me, that no anatomist knew a single one of these particulars and hence made many errors in connection with the larynx.

"Give me, therefore, more attention than if admitted to the Mysteries of Eleusis, or Samothrace, or present at some other holy ceremony, you were completely absorbed by the action and the words of the priest. The action of the nerves resembles both the mechanism of the pulley and the runners in the stadium. I am not able to praise sufficiently the wisdom and power of the One who has created animals. Works so wonderful are above, I will not say praise, but even hymns; before seeing them we would not believe them possible."

# THOMAS SYDENHAM, CLINICIAN*

By DAVID RIESMAN, M.D.

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If the soul of Thomas Sydenham exists somewhere in the cosmos as a conscious essence, it will be surprised to learn with what acclaim the birth of the body that once housed it is being celebrated. In the Old World that it knew, and in the New World of which it knew little, learned societies everywhere are praising the name of Sydenham. In his life he was a modest man, like all the truly great, and cared neither for the plaudits nor the scoffing of men. Why is it that three hundred years after his birth the world does so greatly honor him?

To answer this question it is necessary to understand the time in which he was born and the state of medicine as he found it.

Politically England was in a great ferment. The glorious reign of Elizabeth and the less glorious reign of James I had been followed by that of the incompetent, despotic Charles. The Puritan movement was growing daily, and with it the rebellious spirit in Parliament against an incapable, Constitution-defying government. Eventually civil war broke out between the Parliamentarians and the Royalists. Sydenham's family were native to Dorsetshire, an intensely Puritan county, which Lord Clarendon called the most malignant place in England. No wonder that young Sydenham felt impelled to leave Oxford, where at Magdalen Hall he had matriculated, to take service in the army. Just what he did is unimportant, even were it definitely known. In 1646, when he was twenty-two years old, a chance remark of one Dr. Thomas Coxe, who was ministering to his brother, William Sydenham, a distinguished soldier, led him to take up the study of medicine at Oxford. He was graduated with the degree of Bachelor of Medicine, and was soon afterward installed as a Fellow in All Souls College in place of an expelled Royalist.

* Read January 12, 1925.

Some time previous to 1661 he removed to London and settled in Westminster, becoming a Licentiate of the Royal College of Physicians in 1663. Fellowship in that august body never came to *him*, next to Harvey the greatest of seventeenth century physicians.[1]

A good deal of controversy has arisen about the causes of Sydenham's failure to receive Fellowship in the College, which later placed his bust in front of its doors. One reason undoubtedly was that not having a doctor's degree he could not legally receive Fellowship. Second, Sydenham was indifferent to public honors. Not that he was obtuse to praise or blame. In several places in his writings he strongly denounces his detractors, little wilful men who envied his success in practice and either from jealousy or from lack of insight condemned his views. "Approval of this sort (of his efforts) has little been my lot,[2]" and continuing (the bitter note is evident): "I have weighed in a nice scrupulous balance whether it be better to serve men or to be praised by them, and I prefer the former."

In his letter to Dr. Thomas Short, prefacing the famous treatise on gout and dropsy, he says:

> If this dissertation escape blame both from you and those other few (but tried and honorable men) whom I call my friends, I shall care little for the others. They are hostile to me simply because what I think of diseases and their cures differs from what they think. It could not be otherwise. It is my nature to think where others read; to ask less whether the world agrees with me than whether I agree with the truth, and to hold cheap the rumours and applause of the multitude.

In 1676, when Sydenham was fifty-two years old, he took his degree of Doctor at Cambridge as a member of Pembroke College. His reason for selecting that University rather than his Alma Mater, Oxford, was probably, as suggested by Dr. Latham, that his eldest son had two years previously been admitted a pensioner of Pembroke.

The obscurity in which much of Sydenham's life history is cast extends to a supposed visit to Montpelier. It is believed he went

[1] The experience of Sydenham reminds me of a work by Arsène Houssaye, "The History of the forty-first Chair of the Academy." The French Academy consists, as you know, of but forty members, the Immortals, and Houssaye sketches the history of some of the many men, eminent in literature and art, who deserved but failed to obtain the coveted honor of membership and has represented them as occupants of the forty-first Chair of the Academy. Dr. John Ashhurst refers to this work in his delightful Centennial address before this College, and mentions the names of a number of distinguished men who failed of election to the College, among them Physick, Dorsey, Barton and Gibson.

[2] Works of Thomas Sydenham, London, ii, 117.

there while taking a wealthy patient to the Continent. The great teacher at Montpelier at this time was Barbeyrac, called the French Hippocrates, who may have had influence upon Sydenham. John Locke also studied under Barbeyrac.

When Sydenham came upon the scene, medicine, both as a science and as an art, was showing little progress despite the many centuries that had passed since the time of Hippocrates. As a science it was still under the sway of Aristotle, Galen and the Arabians, although Galen's prestige was rapidly waning in consequence of the publication of Vesalius' *De Fabrica Corporis Humani.* It was the duty of the regius professor of Oxford to read and lecture twice weekly from the text of Hippocrates or Galen.[1] That gives an idea of the medical instruction in England in the middle of the seventeenth century.

Harvey's monumental discovery was given to the world in 1628, but was very slow in winning adherents, particularly in England. Sydenham himself does not once refer to Harvey, although their lives overlapped and they lived in the same city for a number of years. This attitude of Sydenham's is at first sight difficult to understand, but certain facts help us to solve the riddle. Sydenham had no patience with theories and saw little in the speculations founded on the new physiology but carried to an excess not contemplated by Harvey.

In addition to the school that concerned itself with physiologic speculation based at first only on mental processes and not on experience, and therefore distasteful to the practical-minded Sydenham, medicine offered the diverting spectacle of a wordy conflict between two schools, the iatrophysical and the iatrochemical. The latter had as its chief exponent Francis de le Boë Sylvius—he of the Sylvian fissure—an able clinician, abler indeed than those who adopted his theories. Sylvius believed that fermentation was the essence of disease and that it produced either an acidity or an alkalinity of the bodily juices—a simple hypothesis that made treatment simple. All that was necessary was, on the principle of *contraria contrariis,* to bring about a change in reaction. Some echo of this school is discernible in the phrase "uric acid diathesis," so popular a few years ago, and the school has in a sense been revived under a new dress, that of acidosis and alkalosis.

[1] In Oxford the leading professor of medicine in Sydenham's time was Sir Thomas Clayton.

In three hundred years from now, our own cocksure views on these questions will probably seem as fantastic as those of Sylvius and his followers are to us.

The iatrophysists, the opposing school, sprang more or less directly from Harvey's discovery of the circulation of the blood. If it was possible to explain one of the most important functions of the body on a mechanical basis, was it not natural to look for simple physical explanations for all bodily processes?

In many respects this school was superior to the other, and did more for the immediate advancement of medicine. I need only refer to the pioneer work in metabolism of Sanctorio Santoro (1561–1636).

The mechanistic conception was carried to its highest pinnacle by Giorgio Baglivi[1] (1668–1707), who by comparing the arteries and veins to hydraulic tubes, the heart to a piston, the glands to sieves, the thorax to a bellows and the muscles to levers, believed that all functions could be explained on a purely physical or mathematico-physical basis. He forgot entirely that all bodily functions are associated with chemical processes. It should, however, be said to his credit that he did not allow his speculations to govern his practice, and in its exercise gave due heed to the data of experience.

The trouble with those schools was not so much faulty philosophy (in truth, their speculations became the basis of great subsequent advancement), but it was rather their neglect of the fundamental thing in medicine—observation at the bedside. Primarily philosophers and secondarily clinicians, they classified diseases in the seclusion of their studies and not on the basis of sober bedside observation. How far such classification may be carried is perhaps best shown in Sauvage's attempt to arrange diseases after the manner of botanists. As a result he enumerated 2400 different species of disease in his nosology.

William Cullen, the foster-father of the Medical School of the University of Pennsylvania, greatly simplified this cumbersome classification but did not really get rid of the idea of a rigid system.

With the science of disease in such dire straits, the treatment of disease could hardly be much better. Molière, in his caustic satire upon the medical profession, did not overshoot the mark. The men who pompously cited Hippocrates and Galen as the *ultima Thule*

[1] Called "The Italian Sydenham."

of medical knowledge were content with quoting and neglected to imitate the Father of Medicine and the great sage of Pergamos—to study disease in the sick.

Paracelsus, the iconoclast, signalized his first public lecture in Basle by burning the works of the ancients as a mark of his contempt. While he was an acute observer and noted in particular the diseases of mine workers, his descriptions are crude and erratic.

There had been sporadic instances of accurate description of disease from personal observation before the time of Sydenham. Francis Glisson (1597–1677) gave what is even today the best account of rickets, the English disease. Sydenham, however, was indubitably the first real clinician of modern times, the first since Hippocrates to observe and to note the lineaments of disease and to record what he saw with unsurpassed objectivity.

On beginning the study of his works, I was somewhat prejudiced. I had felt that because he had written in Latin, the universal language in his time, his works had had an adventitious circulation and a popularity they would not have enjoyed had they been composed in the vernacular. But I had not read far when I was obliged to change my mind. I now feel that Sydenham deserves all the posthumous fame that he is getting. Knud Faber[1] is right when he says that Sydenham first concisely and clearly gave clinical observation its place of honor as a scientific method, and Chauffard,[2] speaking at the Commemoration meeting of Sydenham's Tercentenary in the Académie de Médecine a few months ago, uttered similar words of praise. Charles Singer[3] calls him the greatest clinical observer since Hippocrates.

Sydenham has been accused of ignorance by some, and of Paracelsian vanity by others, because he does not quote his contemporaries and very rarely the ancients.[4] Neither of these reproaches is to my mind justified. Like Abraham Lincoln, Thomas Sydenham was an autochthon. His feet were planted firmly on the ground. He observed with incomparable eyes, wrote down what he saw in clearest language, and reasoned sanely upon the data of experience, but did not speculate. He reminds me of that laconic marshal of the great Napoleon, who, when an aristocratic subaltern expa-

[1] Faber, K.: Nosography, New York, 1924.
[2] Chauffard: Æsculape, Paris, 1924.
[3] Singer, C.: Legacy of Greece.
[4] Sydenham mentions Hippocrates about a dozen times and Galen only once.

tiated on the achievements of his ancestors, curtly replied: "Nous sommes ancêtres nous-mêmes."

As a clinician, meaning thereby a man who understands the course, the prognosis and the treatment of disease, Sydenham had no rival in his day and I doubt whether later ages have produced one. When he describes the gout or the smallpox, his word-pictures are unsurpassable. What could such a man have gained by dragging in Hippocrates or Galen or Rhazes? I am afraid much of the medical writing of our time suffers from being overweighted with citations of this or that obscure German or French or Scandinavian or Japanese writer. It is refreshing to find a medical essay detailing in simple language the experience and well-reasoned conclusions of an independent thinker. That sort of nonslavish thinking is rather an English trait connected probably with the Englishman's love of liberty, with his independence as a political being.

Heine once said: "The Englishman loves liberty as his wife; the Frenchman as his mistress; the German as his grandmother." A thousand years of that relationship is not without influence upon the modalities of thought.

It is evident from the minute account Sydenham gives of the course of diseases that he either watched at the bedside of his patients with notebook in hand, or recorded what he saw soon after, or that he had a phenomenal memory.

Sydenham drew a sharp distinction between acute and chronic diseases. He sees in disease, particularly in the acute forms, a sort of battle between the forces of Nature resident in the patient's body and the noxious agents. These agents arise within the body in consequence of faulty digestion or faulty mixture of the bodily juices. Diseases are chronic because the reaction of the body against the harmful agent is slow in developing, or because the agent continues to act over a long period. He lays much stress on bodily disposition and age and sex and season and climate, and their influence upon the course of disease. In these various respects Sydenham saw much more deeply than his contemporaries. Sydenham's definition of disease shows a truly remarkable insight. It is as follows: "An effort of Nature, striving with all her might to restore the patient by elimination of the morbific matter."

Sydenham's observations on smallpox are among the best we have. Nothing that a keen mind and the unaided senses could detect escaped him. He shows the difference between discrete and

confluent smallpox, emphasizing the grave prognosis that is signified by a profuse eruption on the face. He clearly describes the secondary fever. "The more the pus, the more the fever." The meaning of convulsions in the offstart of smallpox, as also in other exanthemata, was well known to him:

> I think that thousands of infants have died because their physician was not aware that convulsions of the kind in question are nothing but the forerunner of some eruptive disease, so that as long as practitioners carelessly mistake such symptomatic phenomena for essential diseases, they throw obstacles in the way of the eruption.

His treatment of smallpox brought him into bitter conflict with his contemporaries and led to the accusation of Sectarianism. But that did not deter him, the more so as his results were remarkably good. Stated briefly, the method he adopted was the cooling treatment. In the first few days, he permitted his patients to be up out of bed unless the eruption was confluent; he allowed fresh air to enter the sick room and gave to the parched patients cool drinks "against the act of nurses and lookers-on." It took courage to do this, just as two hundred years later it required courage on the part of Graves, of Dublin, "to feed fevers."

On malaria and ague his ratiocination was exceedingly keen. He speaks of quartan, tertian and quotidian intermittent, and says that the quotidian might in reality be double tertian, a point definitely proved correct over two centuries later.

His description of the severe neuralgia which sometimes is the last symptom of a malarial fever, and his determination of the fact that it really belongs to the disease and must be treated in the same way is a remarkable example of close thinking. The neuralgia is sometimes so severe and so different from what has gone before and so remote from the beginning of the disease, that it seems more like a separate morbid condition; but Sydenham perceived its actual relation to the disease.

Sydenham wrote a short article on the plague, but not from personal experience, for he was not in London during the epidemic. Posterity has censured him for his flight from the stricken city. It must be confessed that in those trying times the leaders of the profession did not set an inspiring example. A few only remained, among them Francis Glisson and Thomas Wharton, the discoverer of Wharton's duct. Poor Thomas Wharton! The king promised him the first vacant appointment of Physician in Ordinary to the

King if he would remain in London and attend the Guards. Soon after the plague had ceased, a vacancy in the promised office occurred and Dr. Wharton proceeded to Court to solicit the fulfilling of the engagement. He was told that His Majesty was under the necessity of appointing another person, but to show his appreciation of Dr. Wharton's services, he would order the heralds to create him an honorable augmentation of his paternal arms. For this empty honor (a canton or, in the dexter quarter) he paid ten pounds.

Sydenham's motives are unknown to us and we can only guess at them. He makes reference to the incident in the following words:

> The danger came to my own doors, and I was persuaded by my friends to add myself to the increasing list of fugitives. I and my family retired a few miles from London. I returned, however, earlier than my neighbors; and, as the calamitous violence of the disease still continued, I was necessarily called in, for the want of a better practitioner, to the relief of the sufferers.

I might perhaps quote one particular paragraph from the article on plague, since it shows how cogently and how profoundly he thought on medical problems. Speaking of sporadic cases of the disease he says:

> I have grown suspicious that the mere atmospheric constitution however much λοιμώδης is by no means sufficient, in and of itself, to originate plague. Either the disease itself must continue to survive in some secret quarter or else, either from some fomes or from the introduction from pestilential localities of an infected person, it must have become extended. And even in these cases it cannot become epidemic, except with the conditions of a favorable atmospherical diathesis.[1]

[1] It is interesting to note that during the Great Plague in London the popular suspicion fell upon dogs and cats as the carriers of infection and these animals were destroyed by the thousands. No attention appears to have been paid to rats (Bell, W. G.: The Great Plague in London in 1665, London and New York, 1924). Yet the classical ages, as Bell reminds us, seem to have had some inkling of the truth, for the God of Plagues was Apollo Smintheus (Apollo the rat destroyer). In Biblical literature (Samuel 1, vi), a reference occurs which is very singular in the light of our present knowledge. The Philistines having defeated the Israelites in battle, they carried off the Ark of the Covenant to their city of Ashod, where thereafter pestilence broke out: "And he smote the men of the city, both small and great, and they had emerods (buboes) in their secret parts." The afflicted Philistines consulted their priests and diviners, who advised that the Ark should be returned to Canaan, and not empty. Then said they: "What shall be the trespass offering which we shall return to him?" They answered: "Five golden emerods, and five golden mice, according to the number of the lords of the Philistines: for one plague was on you all, and on your lords. Wherefore ye shall make images of your emerods, and images of your mice that mar the land; and ye shall give glory unto the God of Israel; peradventure he will lighten his hand from off you."

Sydenham's description of phthisis or consumption is brief but admirable:

> The cough betrays itself. The phthisis comes on between the eighteenth and thirty-fifth years. The whole body becomes emaciated. There is a troublesome hectic cough, which is increased by taking food, and which is distinguished by the quickness of the pulse and the redness of the cheeks. The matter spit up by the cough is bloody or purulent. When burnt it smells fetid. When thrown into water, it sinks. Night sweats supervene. At length the cheeks grow livid, the face pale, the nose sharp. The temples sink, the nails curve inwards, the hair falls off, and there is colliquative diarrhea, the forerunner of death.

It is interesting that a man so keen with his eyes should not have thought of listening to or percussing or palpating the chest, and that more than one hundred years were required for medicine to hit upon those essential methods of investigation.

Sydenham's account of St. Vitus' dance, called Sydenham's chorea in all countries, is another leaf in his laurel crown as a great clinician:

> St. Vitus' dance is a sort of convulsion which attacks boys and girls from the tenth year until they have done growing. At first it shows itself by a halting, or rather an unsteady movement of one of the legs, which the patient *drags*. Then it is seen in the hand of the same side. The patient cannot keep it a moment in its place, whether he lay it upon his breast or any other part of his body. Do what he may, it will be jerked elsewhere convulsively. If any vessel filled with drink be put into his hand, before it reaches his mouth he will exhibit a thousand gesticulations like a mountebank. He holds the cup out straight as if to move it to his mouth, but has his hand carried elsewhere by sudden jerks. Then, perhaps, he contrives to bring it to his mouth. If so, he will drink the liquid off at a gulp; just as if he were trying to amuse the spectators by his antics.

Sydenham's treatise on gout is unsurpassed, as it well might be, for he had himself suffered from the disease for thirty-four years. The essence of the disease is a faulty concoction of the juices of the body, which is about as near as we can come to it at the present day. Only we say proudly, it is a disturbance of metabolism.

Sydenham says gout rarely attacks fools, but modestly adds that "those who choose may except the present writer."

In the treatment of gout he says the man must be made anew:

> It is not as in acute disease, when a person in full health is smit with fever, and falls headlong into a dangerous disease. Gout is different. For years together a man has drunk and feasted—has omitted his usual exercise,

has grown stout and sluggish, has been over studious or over anxious; in short has gone wrong in some important point of life. Whatever the treatment, medicine, diet, exercise, it must not be taken by the by, but must be steadily and diligently adhered to. The patient should keep the mind quiet and not be too intent upon serious matters.

Can you not imagine the influence such a sane counselor must have had on the great and wealthy that came to him for advice? Too many physicians of our own day are content to write a prescription for gout or any other ailment, and neglect to give the far more important advice, "to keep the mind quiet."

As to liquors in gout, those are the best which neither sink to the weakness of water nor rise to the density of wine, such as the London small-beer, either with hops or without hops. First as to wine, the old saw is, "If you drink wine, you have the gout, and if you do not drink wine, the gout will have you.

The first is true enough the prohibitionists could have no better defender than Sydenham. "Water drinkers," he says, "scarcely know what gout is. Indeed, it is the natural drink of the greater part of mankind—more happy they in their poverty than we in our wealth and abundance." That does not prevent him, however, from praising the virtues of Canary wine.

For the benefit of those who may be affected in the same way he was, he gives the following advice:

On getting out of bed I drink a dish or two of tea, and ride in my coach till noon; when I return home and refresh myself moderately (for moderation is the one thing to be always and most strictly observed) with some sort of easily digestible food that I like. Immediately after dinner, I am accustomed every day to drink somewhat more than a quarter of a pint of Canary wine, to promote the concoction of food in the stomach, and to keep away the Gout from the bowels. After dinner I ride in my coach again, and (unless prevented by business) drive two or three miles into the country, to breathe a purer air. [One of his favorite drives was to Acton.]

A draught of small beer serves for my supper, and I repeat this when I am in bed and about to compose myself to sleep. My object in taking this draught is to cool and dilute the hot and acid juices lodged in the kidney; out of which the stone is formed. Both at this time and at dinner, I prefer the hopped, however, thin and mild. For even if that made without hops be better fitted by its greater softness and smoothness to remove a stone already formed in the kidneys; still the hopped beer, on account of the slightly styptic quality which the hops impart to it, is less likely to generate sandy or calculous matter, than that without hops, which is of a more slimy

and muddy substance. On the days when I take a purge, I dine on poultry but drink my Canary as usual. I am careful to go to bed early, especially in the winter, nothing better than early hours to accomplish a full and perfect concoction and to preserve that order and even course of life which we owe to nature. Late hours on the other hand diminish and corrupt the concoctions in old men who suffer from any chronic disease. One precaution I always take to prevent hematuria whenever I drive any distance over the stones (for on the level road I feel no discomfort) is to drink a full draught of small beer upon getting into my coach, and also, if I am out alone, before my return.

Speaking of hysteria he said:

Such male subjects as lead a sedentary life and grow pale over their books and papers, are similarly afflicted, since however much antiquity may have laid the blame of hysteria upon the uterus, hypochondriasis is as like it as one egg is to another. The frequency of hysteria is no less remarkable than the multiformity of the shapes which it puts on. Few of the maladies of miserable mortality are not imitated by it.

In the treatment of disease it was with Sydenham a cardinal principle to interfere as little with the *vis medicatrix naturæ*. He adopted as his own the fundamental concept of Hippocrates, *νούσων φύσεις ἰατροί.* ("Nature is the healer of diseases.")

In actual practice Sydenham used simple, homely methods by preference and, far in advance of his time, would refrain from giving any medicine when the course of the malady was satisfactory.

His only rule in practice was: "What is useful is good." This explains the recourse he at times had to strange proceedings, such as the application of a kitten or puppy dog to get warmth to a patient, or even of a boy or girl as the case might be.

As an example of this method of treatment, we may quote the "Methodus medendi morbos per accubitum junioris" ("putting a child or young person to bed with an invalid"); with the idea apparently that the natural heat of the human body had some specific virtue. Several cases are recorded in Sydenham's own English.

One Mr. Little had a fever about seven weeks, and at the time was so far spent that his doctor judged him a Dead Man. He was ancient, and having been treated with violent medicaments, was as weak as ever I saw any that recovered. Other treatment having failed, I told his wife that nothing could preserve his life but the putting a boy to bed to him. So she procured a Link Boy to lie very close to him all night. The next morning I found his fever almost off, and his eye and countenance more

lively, upon which I pronounced all danger to be over. Yet afterwards, upon the recess of the boy, he began to relapse, but the boy being got again, without any more treatment he perfectly recovered.

The same way he cured Bishop Monk's lady, an aged woman of a very feeble and thin habit of body, so weakened by an ague that the physicians looked upon her as dead. Sydenham told the doctor nothing could save her life but a speedy transplantation of some young spirits upon her. Accordingly a girl, aged thirteen years, was put in close to her breast, upon which she recovered very speedily. Unfortunately the girl fell sick, which was attributed to her lying with the lady; but Sydenham was confident to the contrary and the girl in the end got well.

His honesty is refreshing. He had had success in some cases of dropsy with syrup of buckthorn, so once when he was called to see a patient with the dropsy, he prescribed the syrup. "After a time, as the water remained the same, the lady changed my services for those of another physician, who after my dismissal gave her more appropriate remedies, and cured her accordingly."

Sydenham looked upon fever as a wholesome process, as Nature's way of neutralizing the injurious matter causing acute disease. He therefore did not believe it wise under ordinary circumstances to combat fever. This judicious practice was forgotten, and two hundred and fifty years after him men tried with antipyrin and antifebrin to combat fever.

In his prescriptions he did not depart from the polypharmacy of his time. There is a deal of poetry in his treacles and mixtures, but one pities the poor patient who had to swallow such stuff. For example the Venice treacle, which he used extensively, contained sixty-five ingredients. The famous theriacum was even more complicated, being composed of seventy-two constituents. The preparation of this far-famed remedy required about three months and in Nuremberg the Senate would usually declare a public holiday when it was finished.

Sydenham was fond of emetics and clysters and cathartics, but generally averse to sweat-producing methods.

While not the original introducer of Peruvian bark, he did much to popularize its use; this also applies to laudanum, which he prescribed extensively, always watching the effect of every dose.

Sydenham was a free but not a reckless bleeder, using the procedure as each individual case required. Perhaps he went a little

too far in the case of rheumatism, for Dr. R. Brady in a letter to him says: "In the treatment of rheumatism you have prescribed free and frequent bleedings. I would ask whether some method less prodigal of human blood (and at the same time equally certain) may not be discovered." His views on mineral water also testify to his common sense. This is what he says about them:

> I will now venture an opinion that, although in such waters iron in its soluble principles is present, so that what we drink is neither more or less than iron in a liquid form, the waters themselves are merely simple waters, except so far as they are impregnated with the minerals through which they pass. This will be clear if we only throw some horseshoe nails in a few gallons of common water.

Sydenham discusses venereal disease in a letter to Dr. Henry Paman. In this letter I find that it was not considered in Sydenham's time proper to teach the cure of venereal disease. As in most things, he took the contrary view, and says: "I will state what I have observed and tried in the disease in question; and that not with the view of making men's minds more immoral, but for the sake of making their bodies sounder. This is the business of the physician."[1]

He is against ascribing the origin of syphilis to the American colonies, because the disease was not rarely found to develop in negroes on slave ships before America was reached. Like all men of his day, and for generations afterward, he used mercury up to the point of salivation.

More than any other man of his time, Sydenham laid emphasis upon diet and hygienic measures. Those of us who are today engaged in the practice of clinical medicine can take a lesson from him in this respect. He may not always have been right, but his attention to details, his precise directions, his conviction of the value of the measures he has tried must have carried great weight.

To show his good common sense, I would quote the case of "a gentleman equally favored by nature and fortune," who had had a fever. It evidently left him in a state of profound neurasthenia, for he burst out into a flood of tears at the time of Sydenham's visit.

Sydenham says:

> I laid his complaint partly to the disorder of his spirits, partly to the length of the previous fever, partly to the evacuations that had been necessary

[1] Sydenham's Works, vol. ii.

to his treatment, and partly to the interdiction of animal food by which his physician was guarding against a relapse. I pronounced him free of all fever, and recommended a roasted fowl for dinner, and allowed him a moderate share of wine. This he took, and went on afterwards with animal food in moderation. He never again so suffered.

Once a man in Holy Orders came to me suffering from hypochondriasis as the result of overstudy and overwork. When he consulted me I saw at once that there was no room for medicine. I recommended riding on horseback, at first short rides such as his health would allow.

Had he been a man of less acute judgment, he would never have been induced to try it. He went on and on until he had ridden more than a thousand miles, by which time he had gained perfect health and vigor.

"Riding is as good in decline or in phthisis as in hypochondriasis. It has cured patients whom many medicines would have benefitted as much as many words and no more."

What his opinion might have been of Christian Science and Faith Healing is indicated in the statement that the dogma of the most insolent Stoic will relieve hysterics and hypochondriacs just as much as a toothache is relieved by a resolution forbidding one's jaws to give pain.

While Sydenham had few actual pupils (Sir Hans Sloane and the famous Dover of Dover's powder seem to have been among them), he nevertheless became a great teacher and the founder of a school which persists until our day. His fame spread more rapidly on the Continent than in England, and at the University of Leyden the great Boerhaave took up the methods of Sydenham. From Leyden they traveled to Vienna, then to Dublin and then to America. In Scotland they never took the same foothold, probably because the Scottish mind has a more speculative character.

I must tell the story of Sydenham's answer to Dr. Richard Blackmore, although Munk ("Roll of the Royal College of Physicians") questions its truth. When Blackmore asked Sydenham what books he should read to gain a knowledge of medicine, Sydenham's reply was: "Read Don Quixote. It is a very good book. I read it myself still."

Prof. R. A. Millikan[1] recently said that science walks forward on two feet, theory and experiment. Medicine also walks forward on two feet, observation and experiment—clinic and laboratory. Like physics, medicine has entered on a new era. Not only is the clinical method of Hippocrates and Sydenham carried to a high

[1] Millikan, R. A.: Scribner's Magazine, January, 1925.

degree, but the laboratory, unknown to both men, has become the indispensable handmaiden of the clinical method. Sometimes it seems indeed as if the positions had been reversed, the laboratory assuming to be the more important. That, however, is a false and dangerous situation against which those who call themselves descendants of Thomas Sydenham must protest. The basis of the practice of medicine will always be the study of disease at the bedside by every available method, and since Sydenham is the archetype of those who believe that the most successful way of studying disease is at the bedside, his name will forever endure.

The epitaph on his monument in St. James' Church, Westminster, is magnificent and true:

"Medicus in omne ævum nobilis." A physician famed throughout the ages.

# THE HISTORY OF THE DEPARTMENT OF OBSTETRICS IN THE MEDICAL SCHOOL OF THE UNIVERSITY OF PENNSYLVANIA*

By BARTON COOKE HIRST, M.D.

The early history of the Department of Obstetrics in the Medical School is the history of the heads of the department. It is true that Shippen and James, both trained in Europe, brought home with them a realization of the necessity of providing means for clinical training, but the most that they could obtain was so meager that it was practically negligible and their successors made no attempt in this direction at all. The only teaching the students received, therefore, was from didactic lectures given by the professor. Consequently the success of the department depended entirely upon himself; his reputation; his personality; his ability as a speaker; a striking contrast with the present time when the equipment and organization of the department is everything; the personal qualities of the professor nothing in comparison.

William Shippen, Jr., was born October 21, 1736. His great-grandfather came from the west riding of Yorkshire to Boston, where he acquired wealth and prominence, but he left Boston for Philadelphia, partly on account of the Puritan persecution of the Quakers and partly on account of Penn's pressing invitation to come to Philadelphia, where he filled successively almost all the important offices in the Government.

The Shippen family in England were people of considerable importance; the nephew of the first immigrant was vice chancellor of Oxford University. Shippen's grandfather was a man of wealth and comparative leisure, a friend of Franklin and one of the founders of the Junto. His father, William Shippen, Sr., had the best medical practice of his time in Philadelphia. Young Shippen received a classical education in Finlay's Academy, at Nottingham, Maryland;

* Read March 24, 1925.

finished his education in the College of New Jersey, then at Newark, before its removal to Princeton, and in delivering the valedictory address was so eloquent that the famous evangelist, Whitefield, rose in the audience and publicly complimented him, urging him to enter the ministry.

Shippen obtained his medical education in Europe, going to Great Britain in 1757 when twenty-one years old; he lived with the Hunters in London; studied under William Hewson, Sir John Pringle, Fothergill and McKenzie. In Edinburgh, where he received his degree in 1761, he was instructed by Cullen and Monroe, and having an opportunity to visit France, he came in contact there with the best minds of the profession. On his return to America, in 1762, he gave a course of public lectures on surgery and anatomy in his father's house, in Fourth Street, but the opening lecture was delivered in the Old State House in Philadelphia. On January 1, 1765, there appeared in the *Pennsylvania Gazette* the following statement:

> Dr. Shippen, Jr., having been lately called to the assistance of women in the country, in difficult labors, most of which were made so by the unskillful old women about them; the poor women having suffered extremely and their innocent little ones being entirely destroyed, whose lives might have been easily saved by proper management; and being informed of several desperate cases in the different neighborhoods which had proved fatal to the mothers as well as their infants, and were attended with the most painful circumstances, too dismal to be related! He thought it his duty immediately to begin his intended courses in midwifery, and has prepared a proper apparatus for that purpose, in order to instruct those women who have virtue enough to own their ignorance and apply for instruction, as well as those young gentlemen now engaged in the study of that useful and necessary branch of surgery, who are taking pains to qualify themselves to practice in different parts of the country, with safety and advantage to their fellow-citizens.

After giving an outline of the contemplated course, the advertisement goes on to state that:

> In order to make the course more perfect, a convenient lodging is provided for the accommodation of a few poor women, who otherwise might suffer for want of the common necessaries on these occasions, to be under the care of a sober, honest matron, well acquainted with lying-in women, employed by the doctor for that purpose.

This was the beginning of the Obstetrical Department of the University of Pennsylvania and its Maternity Hospital, the first

of its kind in America, for in September, 1765, Shippen was appointed professor of anatomy and surgery in the Medical School of the College of Philadelphia, the precursor of the University of Pennsylvania. Curiously enough, the title of professor of midwifery was not added to his titles of professor of anatomy and surgery until 1793, although his predilection had always been for obstetrics, which he studied with particular attention in London and Edinburgh. His graduation thesis was entitled, "De Placenta cum utero nexu." In fact it was not until 1813 that the professor of obstetrics, then Dr. James, had a seat in the faculty and the course in this subject was made obligatory, an evidence of the strange indifference that so long prevailed to a branch of medicine not exceeded, if indeed it is equalled, in its importance to the individual, the family and the State.

Shippen continued to teach for forty-one years, but during the Revolution he naturally devoted his attention more to military affairs. He was appointed director general of all the military hospitals in the United States during the Revolutionary War. He died July 11, 1808.

He was succeeded in the chair of anatomy and obstetrics by Caspar Wistar in 1808; but Wistar, who was interested only in anatomy, soon petitioned the trustees of the University of Pennsylvania to create a separate chair for obstetrics, which was done in 1810, and the first incumbent elected to this position was Thomas Chalkney James, born August 31, 1766, and graduated in medicine in the University of Pennsylvania in 1787. He then took a sea voyage, as surgeon, around the Cape of Good Hope to China, in order to obtain funds to continue his medical studies in Europe.

He spent three years in London and Edinburgh, returning to Philadelphia in the midst of the yellow-fever epidemic in 1793; a year later he accompanied the MacPherson Blues as surgeon on their Western military expedition. In spite of professional learning, extensive travel, military service, excellent social and professional position, he was remarkably shy and retiring, hesitating to express his views authoritatively and leaving little behind him commensurate with his learning and experience. He was the first in America, however, deliberately to induce labor for a contracted pelvis at the conclusion of the seventh month with success for both mother and child. This was in 1810. Eight years previously he had established a practical school for obstetrics in the wards of the Philadel-

phia almshouse; sections of three students attending each delivery. In 1827 he argued in favor of abdominal pregnancies always being secondary. He had considerable literary ability, but was so diffident that what he wrote was published anonymously. He thus contributed a number of poems to contemporary magazines.

He was a man of profound religious conviction. He mastered a number of foreign languages, so that he might study his Bible in Hebrew, Greek, Latin, French and German. His chief literary work in medicine was his adaption of Burn's book on *Obstetrics* for the use of American medical students. He died in 1835.

The associate and successor of James in the chair of obstetrics was one of the most remarkable figures in American medical history.

William Potts Dewees was born May 5, 1768, of Swedish ancestry on his father's side, of English on his mother's, who was the daughter of Thomas Potts, of Pottstown, where Dewees was born.

He began the practice of medicine after attending only part of a course of lectures, without acquiring a degree, at first settling in Abington, a few miles outside of Philadelphia. He came to the city directly after the yellow-fever epidemic in 1793, and without influence, self-educated, without any of the advantages which his predecessors had enjoyed, but by the force of his genius and mental power he immediately achieved an astounding success.

He received his honorary medical degree years after he had been in practice. He had instructed himself in French and Latin and was mainly influential in introducing Baudelocque's work to American students. At the age of forty-four he retired from practice to conduct a farm in the country, in which enterprise, like so many physicians in business, he lost his whole fortune. He returned to Philadelphia five years after he had left the city, poor and with a large family dependent upon him. He immediately resumed the successful practice he had left five years before. His literary fecundity was amazing. The numerous editions of his works on obstetrics, diseases of women, practice of medicine and diseases of children were the authorative books on those subjects in America.

The dedication of Hodge's *Obstetrics* to him and to James expressed the feeling of the profession: "To the Memory of Thomas C. James, the first professor of obstetrics in the University of Pennsylvania, and of William Potts Dewees, his colleague and successor, by whose talents and attainments, moral excellencies, social influences, public teachings and classical writings, the foundation of the science of obstetrics was made in America."

Dewees' reputation was not confined to this country. He was the first to confer dignity on American medical literature. Ramsbotham dedicated a book to him; Rigby wrote that he was a close student of his work and his books were translated into German. He died in 1841.

He had a worthy successor in Hugh Lennox Hodge, born in 1796. His early career was devoted to surgery, but on account of failing eyesight he was compelled to adopt obstetrics as his special work. He taught this subject for thirty-one years. He is accorded world-wide recognition as one of the notable contributors to the advancement of the science and art of obstetrics. His book is read to-day with respectful attention. We owe to him the foundation of our knowledge of the mechanism of labor and of the pelvic planes. To my mind there is no work on obstetrics of his time in any language comparable with Hodge's book. He died in 1873.

His successor, Richard A. F. Penrose, born in 1827, died in 1908, in his eighty-first year. He graduated at Dickinson College, 1846, and from the medical department of the University of Pennsylvania in 1849. In 1854 he was consulting physician to the Philadelphia Hospital and was one of those who opened the wards of that hospital for instruction to students. He was one of the founders of the Children's Hospital and of the American Gynecological Society.

In 1863 he was the fifth professor to occupy the chair of obstetrics and diseases of women and children in the University of Pennsylvania, having been preceded by Shippen, James, Dewees, Wistar and Hodge. He resigned in 1889. Penrose wrote very little. His greatest claim to distinction was his brilliant career as a didactic teacher. Before the days of the obstetric clinic, Penrose with his manikin, Mrs. O'Flaherty, of blessed memory to the class of forty years ago, actually gave clinic instruction of the highest order, and enacted the drama of labor and its complications with the accomplishments of the trained actor and skilled orator.

His dramatic conversations with his padded manikin, his wit, humor and profound knowledge of human nature, his flights of oratory that thrilled his audiences and carried a pointed lesson in practical obstetrics—who among his students could ever forget them?

His lectures were carefully written and committed to memory, and yet his art made them appear wholly spontaneous. He taught practical obstetrics only. Being profoundly convinced that his views were correct, he made his classes believe that his was the last

word to be said on any topic he presented. He was sure of his teaching and he made his students sure of the knowledge he gave them.

On Dr. Penrose's resignation the chair of obstetrics was divided for one year between Dr. Howard A. Kelly and the present incumbent, who, the following year, was put in sole charge of the department. He was confronted with a serious, not to say discreditable situation and a formidable task. His sole equipment for teaching was the use of a lecture-room for an hour, three times a week. From that time on the history of the department ceases to be that of an individual; it becomes the record of a developing equipment and organization that has resulted in conditions so familiar to our present students that their detailed description is superfluous.

# THOMAS DENT MÜTTER

## Professor of Surgery, Jefferson Medical College, 1841–1856*

By JOHN H. GIBBON, M.D.

During the first half of the last century Philadelphia was the medical center of America, and deserved the distinction, for in no other city during this period was there such a combination of distinguished teachers, writers and investigators. Her medical schools during the latter half of this period had in the their classes students not only from every state and territory in the Union but from many foreign countries. During most of this period there were more than one thousand medical students in Philadelphia. Her teachers were men of distinguished ability, refinement and culture, were well educated and produced many textbooks of merit, and were familiar with the literature of their own language and that of France and Germany. It is striking to see how many of them began their literary efforts with translations of French and German works. This occupation was one of the "pot-boilers" of the ambitious young man of those days, helping him over the first hard and uncertain years, and doing much to make him known at home and abroad. Notwithstanding the time and expense entailed, many of these men had been educated in the best foreign schools (that of Edinburgh being the most popular), or had supplemented their studies with postgraduate work in the great medical centers of Paris, Edinburgh, Berlin and Vienna.

The early fame of Jefferson College was not a little due to the men who occupied its chairs of surgery and anatomy: McClellan, Pancoast, Mütter and Gross, names familiar to all medical men, and no history of American medicine has ever been, or ever will be, written that does not give due space to their accomplishments. It is interesting to note that two of the four, Pancoast and Gross, were succeeded by sons and that McClellan's grandson later occupied the chair of anatomy. Mütter died childless.

* Read March 24, 1925.

When it was suggested to me to write of the early surgeons of Jefferson, Pancoast and Gross came first to my mind; but on reflection I concluded to choose but one and determined finally on Mütter, because less has been written about him, possibly because he wrote comparatively little himself. It is probable, however, that except for ill health and an early death surgical annals would contain more contributions from his pen. This does not mean that he did not report his work and publish his opinions. His contributions will be referred to later. He is known to the medical world today largely through two foundations, which he established a few years before his death, the Mütter Museum and the Mütter Lectureship; yet his life and activities hold many other interests for the student of medical history.

Thomas Dent Mütter was born in Virginia in 1811 of Scotch and German ancestors. His grandfather, Thomas Mütter, who came from Scotland, settled in North Carolina and married a Miss Moore, a member of an extensive and influential family in the South. Members of both the Mütter and Moore families rendered distinguished services to their country during the Revolution, especially in opposing the march of Lord Cornwallis' army through the Carolinas and Virginia. A great uncle, George Mütter, was a colonel of artillery and later became Chief-Justice of Kentucky. John Mütter, the father of Dr. Mütter, was sent by his father to Scotland to be educated and on his return he settled in Richmond, Virginia, as a factor and commission merchant. He married Lucinda Gillies, who died in 1813, two years after the birth of Thomas Dent Mütter. The father four years later developed tuberculosis and taking his secretary and a physician sailed for Europe in 1818, made a winter passage of the Alps and arrived at Naples, where he died in 1819, leaving his son and only child an orphan at the age of eight years. Mr. Robert Carter, a relative of the boy's mother, became his guardian and took him to his seat, Sabine Hall, in Richmond County, Virginia. He was sent later to Hampden-Sydney College in Virginia and afterward to the University of Pennsylvania to study medicine. Here he graduated in 1831 at the age of twenty years. At the termination of his medical course he found himself in frail health and decided to go abroad, with the double object of improving his physical condition by a sea voyage and his mind by a course of study in Paris, where were to be found the most advanced and most distinguished men in the

surgical world. Their influence was deep and indelible and showed itself in all the subsequent activities of the young American. No young man of intelligence and discretion, wishing to increase his knowledge and improve his culture, could have failed to do so in Paris during the reign of Louis Philippe. To one in his early twenties, passing from this quiet Quaker town to that environment of science, art, literature, music and alluring vice, the change must have seemed like that to another world. The transient American has always misjudged the French capital and usually the French race, but what these patriotic people have done in the past ten years has given us a more correct idea of the French character. This fine exhibition of her faith, her strength and her sacrifice should not have been necessary to show the world her true character, for has she not for generations been a leader in the arts and sciences of peace as well as of war? At the time of which we are speaking, she was undergoing a new birth. The men who were bringing this about were in every line noted for their intellect and their learning. Paris was the medical Mecca and was full of students and graduates from all parts of the world.

There was hardly a man occupying a teaching position in medicine in Paris at this time whose name and work are not familiar to us today. Some of the surgeons were Nélaton, Marjolin, Roux, Chassiagnac, Dupuytren, Lisfranc, Ricord, Malgaigne, Sappey, Velpeau, Larrey (*père* and *fils*) and Lembert. Teachers in other branches were Trousseau, Louis, Gay-Lussac, Lugol and Baudelocque. What an impression such a galaxy must have made on our embryo surgeon and what an inspiration they must have given him! The young man also spent some time in England and profited by his brief contact with her great surgeons. Later in life he made other trips abroad.

It is quite astonishing that this young man in less than ten years should have found himself full professor of surgery in Jefferson College and a colleague of Robley Dunglison, Joseph Pancoast, Charles D. Meigs, John K. Mitchell, Robert M. Huston and Franklin Bache. These seven men constituted the faculty for fifteen years and there has rarely been a more distinguished one in America. I can remember as a boy my father telling me of being sent by his father, a graduate of the University of Pennsylvania, to Philadelphia in the early forties to study medicine at the University and how he fell under the spell of the men whose names I have

just mentioned and so decided to enter Jefferson. He often spoke of the attractive Mütter and told me how he had been examined by the professor while they sat together in his carriage and rattled over the cobble-stoned streets. All the members of this faculty had their attractions for the student. Mütter was not the most distinguished, he was not the best surgeon, he was not the best or the most frequent contributor to surgical literature, but he was a most popular teacher, not only because of his personal attractions, features, voice and bearing, but because he was enthusiastic and always endeavored to make his lectures interesting and comprehensive. It has been said that he "played" for popularity, but few of his contemporaries were free from this fault. I am afraid it is a thing not altogether unknown or unpractised today, but I suppose at no period in our medical history was rivalry so marked with jealousy and unfairness. Medical lore and literature contain ample evidence of the personal abuse and criticism which medical men showered upon one another and of the acrimony which characterized the discussion of important questions, especially that of treatment. The same conditions existed abroad and I think the old world has been slower to drop this type of acrimonious discussion and unwarranted jealousy than we have in America. Gross in his autobiography tells an amusing story which is apropos. A certain English scientist, after a visit to the great von Haller at Berne, met Voltaire in Paris, who spoke very highly of the character, abilities and accomplishments of the eminent Swiss. The Englishman replied: "You speak better of him than he does of you," whereupon, with a shrug of his shoulders, the great Frenchman retorted: "Perhaps we both are mistaken."

I am convinced that one of the things which made for the success of the young rival of the University and which did much to insure her future was the comparative good feeling which existed in the faculty of Jefferson between the years of 1841 and 1856. The feeling between the two schools also began to improve, and with the added magnanimity of an Agnew and a Gross, in later years, it was largely eliminated as far as the faculties were concerned, though the students in the two institutions, individually and collectively, have at times brought forward in an unparliamentary way the good and bad points of both. Any institution is sure to suffer from internecine spats in its governing body or faculty and, although I am putting forth no claim that Jefferson was freer of them than any

other medical school (she certainly had had more than her share from her foundation in 1825 by that well-known fighter, George W. McClellan, up to the inauguration of the faculty of 1841), yet I have been interested in studying the lives of her surgeons to observe their cordial relations. We are told that Mütter, who was of course much younger than Joseph Pancoast, the professor of anatomy, and by no means so skillful an operator, would, whenever he had a serious or difficult operation to perform, call upon his colleague for help and support, which was always readily given. Pancoast speaking of Mütter said: "My well-known friendship for him, from our close, affectionate, I may also say, unclouded intimacy of twenty years' duration, etc.," and again, "It is the sweetness of his character which I love most to recall." Pancoast's eulogy of Mütter gives us not only a picture of the one but an idea of the flowery style of the other:

> He felt it a glorious thing to be able to rescue a patient from present suffering or impending danger, when everything else had failed, by the achievement of a successful surgical operation. He loved, by close investigation and careful comparison with all his previous experience, to match himself with the most difficult cases. He carefully prepared himself, even in the minutest points, for the difficulties he had to encounter, and then, with equal skill and firmness, with a sparkling eye and dilating faculties, advanced to the task, more like (than anything else with which I can compare him) to a warrior in the lists, with a white plume dancing on his brow, with spur on heel, and poised lance, his courage aroused with the danger, and his pulse stirred with the energy of the strife.

The relations too between Mütter's successor, Samuel D. Gross, and Joseph Pancoast were always most cordial and friendly, each having a genuine appreciation of the other. Of Mütter's personality Gross says:

> In his dress he was the pink of neatness; and there was that dash, enthusiasm, earnestness, and action about him which never fail to elicit attention and create popularity. He was of medium height, slender and graceful in form, with light eyes and a handsome forehead. His voice, remarkably clear and distinct, had unusual strength and compass. In 1851, during my temporary residence in New York, I made a three days' visit to Philadelphia, purposely to hear the more distinguished teachers lecture; and there was not one of them in the two great schools who impressed me more pleasantly as a good speaker than Mütter. He appeared to be thoroughly familiar with the subject of his discourse, and every member of the class was seemingly an attentive listener.

As has been said, Mütter's contributions to surgical literature compare unfavorably both in extent and character with those of his contemporaries. He published a monograph on the treatment of clubfoot and brought out an American edition of Liston's *Surgery*. He also reported many of his cases and published some of his lectures. The *American Journal of the Medical Sciences* between 1841 and 1856 contains a number of his contributions.

On his return from Paris young Mütter must have "cut quite a swath" in Philadelphia as he drove about her streets in a low carriage behind a big gray horse, driven by a servant in livery. But we are told that notwithstanding these auspicious phylacteries his progress was not rapid. He probably was a little too full of his French masters and talked about them a little too much. But he was serious, sincere and ambitious, and after a while, when he had been teaching surgery in the Philadelphia Institute, a summer school, as an assistant to Dr. Thomas Harris, he established a reputation as a lecturer of no mean ability and as a surgeon of judgment and skill. In our profession, the two incentives which have been most productive of great results have been ambition and poverty. Mütter had the first and if the sting of the other had been sharper he would probably have had to resort more strenuously to that "pot-boiler" already mentioned and would have left behind him a more indelible impression. His forte, as a surgeon, seems to have been in reparative surgery, largely learned in Paris. He was celebrated for his operations for clubfoot and other congenital defects, such as hare-lip, and for his plastic work on the deforming contractures from burns and injuries. A perusal of *Liston and Mütter on Surgery* will give one a good idea of his style. It is quite interesting to read his details of operations, especially the long and tedious plastic ones done on the face without an anesthetic. Today these seem incredible. Quickness and dexterity were essential to the successful surgeon of that day and Mütter's ambidexterity must have proved of value to him. He laid great stress on the importance of the preparation of his cleft palate cases for their ordeal and also on the after-care of these cases. As there was no anesthetic, he had to have some coöperation on the part of the patient, so one of the things he considered necessary was the accustoming of the parts to manipulation. This was done by touching the palate with instruments and fingers over a number of days before the operation. He insisted that the patient should not

speak for some days after the operation and attributes the cutting of some of the stitches in one of his reported cases to the fact that the patient talked in his sleep.

Mütter was an advocate of trephining for hemorrhage in head injuries, where a diagnosis could be made, and gives an excellent description of rupture of the middle meningeal artery.

He operated successfully for epilepsy of three years' duration, due to a depressed fracture of the skull. The case was reported by "My intelligent young friend, Doctor Squibb," he of subsequent ether fame.

In noting the paucity of Mütter's publications one regrets that he wrote nothing of his year in Paris. An idea of that great city in the thirties, from a medical viewpoint, can be found in the accounts of William Gibson, professor of surgery at the University of Pennsylvania when Mütter occupied the chair at Jefferson, and of J. Mason Warren, of Boston. Mütter, however, might have looked upon the French life and her savants in a way differing from that of either Gibson or Warren.

At the time of his retirement from the faculty (1856) Mütter had accumulated a remarkable collection of anatomical and pathological specimens and of illustrations of morbid processes. Evidently the time his colleagues spent in writing, Mütter spent in collecting, and he has left a monument, the Mütter Museum, which will perpetuate his memory. If the Jefferson College had been able to properly and safely house this collection, she would probably be its possessor today; but Mütter before leaving this country for Italy, the climate of which he hoped would benefit him, wrote the College of Physicians of Philadelphia:

> In consequence of ill health, I find myself obliged to resign, for a time at least, the office and duties of a teacher of surgery. With the view of rendering some return to my profession for the benefits derived from its prosecution for so many years, and, above all, to serve at once the cause of science and of humanity, I have determined to found a pathological museum which shall be open to all physicians and to all students of medicine without fee or charge of any sort. I herewith offer the guardianship of this museum to the Philadelphia College of Physicians as the body best qualified by the character of its members and the nature of its pursuits for undertaking the trust.

He insisted that the collection should be housed in a fireproof building. This condition the College was not then prepared to meet, but with the completion in 1863 of its new building at Thirteenth and

Locust Streets, the Mütter Museum was properly installed. Dr. Mütter had in December, 1858, three months before his death, signed an agreement with the College to turn over his collection if the College could comply with the condition within five years.

An inventory of the collection sent from the Jefferson College to the new fireproof building of the College of Physicians in 1863 showed: 474 bones, 215 wet preparations, 200 casts, 20 wax preparations, 8 papier-maché models, 5 dried preparations and 4 oil and 376 water-color paintings.

With this custodianship came a gift of $30,000.00 for the care of the Museum, for the purchase of additions and for the establishment of a lectureship. The College has faithfully carried out this trust and the Mütter Museum and the Mütter Lecture are known throughout the medical world.

Dr. Mütter married Miss Mary Alsop, of Middletown, Connecticut. They had no children. The cause of the ill health, which forced him to resign his professorship, is usually given as gout, but Pancoast tells us he had numerous pulmonary hemorrhages and that he passed the winter of 1856 at Nice, hoping that the warm climate would prove of benefit. On his return he went to Charleston, South Carolina, where he died March 19, 1859. He is buried in Middletown, Connecticut, where his devoted wife erected a church to his memory.

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# CURIOSITIES FROM THE COLLECTION OF CALCULI IN THE MUSEUM OF THE ROYAL COLLEGE OF SURGEONS*

By ALEXANDER RANDALL, M.D., F.A.C.S.

We are prone in our modern atmosphere of precision, in urology to overlook the difficulties and trials of the surgeons of the elder day—their perplexities and yet their wonderful diagnostic intuition, their uncertainties and yet their profound faith and marvelous perseverance, their surgical handicaps and yet their remarkable speed, dexterity, skill and astonishing results; all these should be constantly brought back to us as incentives to do better work with our tremendous modern advantages. And are we not also too apt to form our judgment of their abilities as though they were our contemporaries? The precept, "Never judge your fellow-man until you find yourself in a position similar to his," could not be better applied than when we undertake an appreciation of their work in their day. So to equalize the sphere of the surgeons which I am about to present to you and our time, absolve yourself of any knowledge of the *x*-ray and the cystoscope, of ether and chloroform, of the electric lamp and even the oil lamp; purge your mind of your knowledge of and familiarity with the open peritoneum, of asepsis, of hemostasis and of antiseptics; forget there are such things as rubber drainage-tubes and flexible catheters, and then listen to the exploits and successes of the early lithotomists.

What impresses you first, in reading of their work, is the enormous number of operations they were able to perform. It is true, of course, that where there was one in their day there are ten today; but, on the other hand, the density of population was less, travel was limited and slow, and the dissemination of knowledge was slower. A second impression that repeatedly startles one is the remarkably low mortality that attended such a serious and vital

* Read March 24, 1925.

operation as lithotomy. Speed was considered an absolute essential and was so highly developed and so thoroughly instilled that today we are just emerging from under its dominant law.

Cheselden performed 27 lithotomies without a death, lost his twenty-eighth patient and then continued with 31 more without mortality. A record one would be proud of today.

Le Cat, by the lateral operation, in seventeen years' time operated upon 157 without a death and a second series of 90 without mortality.

Jacob van Diden, of Utrecht, had only 4 deaths in 100 operations, and 66 in succession without a death. It is of interest that he wounded the rectum in 3 of these, but all of them healed.

Then there is Frère Jacques, that picturesque itinerant monk, hounded out of France because he had 23 deaths in 60 cases. Wandering to Holland, he there perfected his operation and returned to France to obtain complete recognition after performing 38 operations and obtaining 38 cures. Frère Jacques is credited with having performed 4500 lithotomies. One of the most amusing incidents in his hectic career was when he was called to operate upon the Maréchal of Lorges. He found the old gentleman loath to submit until the operator's skill had been proved upon some of the lesser lights in the court; Frère Jacques thereupon performed 22 lithotomies without losing a single case; the Maréchal then submitted and promptly died the day following his operation.

The first catalogue of calculi contained in the Museum of the Royal College of Surgeons was made in 1842, at which time 600 specimens were in the collection. A second catalogue was made in 1871 and covered 1005 calculi, the vast majority of which have been analyzed chemically and from this wealth of material valuable deductions have been drawn. It was shown, for instance, that uric acid or its salts formed the nucleus of calculus formation in eleven-fifteenths of all specimens; that ureate of ammonia in its pure state is peculiar to early life, being seldom if ever found after puberty. The accuracy of the general law laid down by Dr. Marcet, that the phosphatic diathesis is never succeeded by any other, is fully borne out by the examination of this collection, and once the phosphate of lime, ammonia and magnesia (often mixed) starts to form they are rarely succeeded by other deposits. The collection shows no instance in which the phosphates form the nucleus of a calculus. That uric acid calculi can undergo partial solution

while in the bladder is proven by several specimens; and the pure uric-acid calculus is the one that occasionally undergoes spontaneous fracture.

Each calculus in the catalogue is accompanied by a brief history, a chemical analysis and the name of the donor, and I have picked out a few unique for history, operation or character of stone formation, hoping that they may interest you as they have me.

Repeatedly, we will find specimens removed and donated by the famous operators of their day, for it must be remembered that the field of surgery was limited and lithotomy represented one of the few major operations advised and voluntarily undertaken, and where accident or emergency played no part. The quaint English and the expressions used, often so descriptive, are likewise worthy of your attention.

C 7. A large and characteristic specimen of the mulberry calculus, having the following curious manuscript memorandum by Sir Hans Sloane:

"This stone was given me by Mr. Pearce, who assisted while it was cut out of the bladder of a sailor, twenty-nine years of age, in St. Bartholomew's Hospital, in the year 1717, by Mr. Salter. He was a lusty, strong, hardy fellow. The pain in his bladder was not great until two days before he was cut, but during these it was very acute and probably the tubercles at the surface were formed during this time; indeed the whole seems not to have been long in formation. There is a nucleus or central body, about which the incrustations were successively formed; they are irregular, and as it were curled or undulated. The urine seems to have been in ebullition when the whole, and especially when the tubercles, were formed. None but a fellow so hardy could have borne such principles in him, abid the formation of such a stone, or indured the cutting of it out, all which yet he bore well, recovered, and went away in good health to sea."

Cc. 51. A globular-shaped calculus having three projections composed of phosphate of magnesia and ammonia.

"Taken from the bladder of a young man who had long been laboring under symptoms of stone. The bladder was contracted, thick-walled and fleshy; its mucous surface was thick and corrugated, full of crypts and large muscular bands stretched across its surface. The calculus was lodged in a deep excavated cupped ulcer in the front of the trigone vesicale just behind the urethra; and its three projections corresponded with the three openings of the bladder, viz., the urethra and the two ureters."

Presented by James Salter, Esq., 1864.

Here is an instance of success and true gratitude:

A 214. Section of a large uric calculus, "containing merely traces of earthy matter, chiefly oxalate of lime. It weighed when entire, six and a half ounces troy." Extracted by operation from the bladder of a Hindoo, twenty eight years of age, a Brahmin by caste, by George Coles, Esq.

"The patient suffered for many years from urinary symptoms of a most distressing character; these latterly so much increased as to render him incapable of bearing the motion of a horse, and unable to do any kind of work; his sleep was also much disturbed. The bladder was not diseased; the prostate was not enlarged or indurated. There was no great difficulty in extracting the stone. The patient had no bad symptoms after the operation; he recovered in one month and sixteen days, and walked from the Indus to Lahore, a distance of 240 miles, in order to see Mr. Coles a year after."

Presented and analyzed by Bransley B. Cooper, Esq.

You are curious as regards operative fees in those days? Here is one recorded:

A 264. A large uric-acid calculus, which at the present time and after division weighes two ounces seven drachms.

"Cut from James Clitherow of Boston House, 13th of August, 1680, then aged sixty-two. Clitherow died November 25, 1682."

The following curious statement of expenses attending the operation was taken from his books and sent with the stone:

"To £150 paid by agreement to Monsieur Callot ye Frenchman for cutting me of the stone. To Apothecary, Surgeon and Nurse, that attended me £28 15s. 2d. For a pallet bed and ye furniture of it then used £6 17s. For charges of removing to and from London £1 10s."

Presented by George Cooper, Esq., 1866.

(Total $933.00.)

Encysted or diverticulated calculi were probably rarely recognized and often overlooked in those days before the *x*-ray, though the following graphic description leaves nothing to be asked:

B f 8. Half of a large calculus, the greater part of which consists of uric acid, deposited upon a small nucleus of urate of ammonia mixed with oxalate of lime. The calculus, when entire, weighed three ounces and a quarter (Av.). Extracted, by the lateral operation, from a boy fourteen years of age, a patient in the Middlesex Hospital, by Mitchell Henry, Esq. The boy had suffered from symptoms of stone during two years; he quickly recovered.

"Considerable difficulty was experienced in removing the stone, arising partly from its large size, and partly from the fact that it was adherent to the upper part of the bladder. This was shown by the fact that when the stone was drawn down by the forceps, and then suddenly let go, the rebound of the stone and of the bladder into their natural positions could be distinctly felt by the hand placed upon the abdomen; moreover it was only when the forceps was directed upwards, and to the right side, that the stone could be seized. Presented by Mitchell Henry, Esq., 1858."

Hernia of the bladder with calculus is found in the next specimen:

H 34. A fusible calculus which was contained in a portion of the bladder that protruded through the abdominal ring into the scrotum, and was removed during life by Mr. Percival Pott. The calculus is surrounded by the portion of the bladder which formed the cyst. The following history of the case has been abridged from Mr. Pott's *Chirurgical Works*.[1]

"A boy about six years old was seized with an acute pain about the region of the pubes: it lasted near an hour and a half, and suddenly ceasing he became perfectly easy. During the time his pain lasted he could not discharge a drop of water, though he endeavoured so to do, but as it ceased he pissed freely. In a few days after a small tumour was discovered, about the size of a pea, in the spermatic process just below the groin; it gave the child no pain, and therefore no notice was taken of it . . . When about thirteen years of age the boy was examined by Mr. Pott, who found the swelling to be perfectly equal as to its surface, indolent, and of a stony incompressible hardness; it was troublesome from its weight, but never occasioned pain in the back or loins: it had every appearance of being dependent from the spermatic process, which was larger than natural, although the cord had neither the feel nor the appearance of being diseased. As the tumour was now troublesome upon motion, and manifested a disposition to increase in size, it was resolved to remove it. An incision was therefore made through the skin, and cellular membrane, the whole length of the process and scrotum, when a firm white membranous bag or cyst was exposed, connected loosely with the cellular membrane, and which, on being traced upwards, became narrower, and was found to be dependent from, and continuous with, a membranous duct, about the breadth of the largest wheatstraw, or what it was more like to, a human ureter muscle. The testicle lay immediately behind the tumour, and was small, flat, and compressed. On dividing the duct immediately above the tumour, about four ounces of a clear fluid issued, and the mouth of the cyst expanding itself, disclosed a stone exactly resembling what is found in the human bladder. In order to be certain that the cyst was connected with the bladder, the boy was desired, after some time, to make water; when a large stream of urine flowing through the wound, instead of the urethra, put the matter beyond all doubt. The patient was dressed superficially; he had no bad symptoms, his urine came through the wound in his groin for about a fortnight, but as the wound healed it resumed its natural course; since which time he has remained free from complaint, except that the natural size of the bladder being lessened by the extirpation of a part, he is obliged to discharge his urine rather more frequently."

Presented by Henry Earle, Esq., 1818.

That symptoms of stone may abate over long periods is not generally conceded, yet here is one of thirty-three years' duration:

[1] Pott, P.: Chirurgical Works, 1775, p. 789.

C 64. An oxalate of lime calculus, having an oval figure which weighs one ounce and a half. It is a very dark colour, and is highly tuberculated on its external surface. Extracted, by operation, from the bladder of a man forty-five years of age, a patient in Bucks Infirmary, by James H. Ceely, Esq. The man, when fifteen years of age, suffered pain in the hypogastric region, extending along the urethra to the glans penis; during the succeeding twelve months, the pain was very violent at intervals, and was followed at each attack by the evacuation of bloody urine. Since that time he occasionally experienced pain in these situations when taking horse exercise, or during unusual exertion, but never to any great extent. With these exceptions, his general health, although delicate, had been good until three months before his admission to the Hospital, when he had an accession of symptoms similar to those already mentioned, but greatly aggravated, the urine, in addition to blood, containing gravel. The patient was discharged perfectly well one month after the operation.

Presented by James H. Ceely, Esq., 1865.

I have mentioned that speed was essential to success in operating in these pre-anesthetic days, and it is remarkable to what extent it was developed.

A 215. A large uric acid calculus, of a flattened oval figure, which weighed four ounces troy.

"Extracted in two minutes from the bladder of an Indian artisan, aged forty, by Thos. Atchison, Esq. The patient recovered. A simple incision was made; the urine passed through the urethra on the fifth day after the operation."

Presented by Thos. Atchison, Esq., 1857.

Cheselden is said to have done a lateral lithotomy in twenty-four seconds and seldom took longer than one minute for a single stone: in proof of which we find:

A 110. An undivided uric acid calculus, finely exhibiting the tuberculated exterior; it is inclosed in a box, on the lid of which is engraved: "This stone was extracted by William Cheselden, Esq., from William Nightingall, on April 20th, 1737; its weight six ounces and a half, and in circumference nine inches; the operation was effected in half a minute."

Such careful safe-keeping was not unique in family archives and the surgeon's efforts were often considered worthy of careful record and preservation.

Thus we find the following specimen also:

B d 3. A small oval calculus, contained in an oval silver box, with the family arms engraved on the lid, and the following inscription on the outside:

"Deliverance was sent from God to Francis Godman, the 26th September 1687, in the 7th year and 10th day of his age."
Presented by F. G. Capell, Esq., 1823.

There are numerous unique and rare specimens, and I will present some without comment:

F 7. Calculus matter lining the interior of a "sac connected with the bladder of King George IV." Museum of Sir Astley Cooper, Bart.

One case of pilimiction is recorded with calculus formation:

H a 16. Earthy phosphates mixed with and apparently deposited upon hairs from the bladder of a woman.
Presented by Joseph Hodgson, Esq., 1866.

A 75. Presents a large calculus, consisting of uric acid with a very thin layer of the mixed phosphates on its exterior: this calculus was accompanied by the following history in the Sloanian Catalogue, although from its size it is scarcely credible, being two inches, and an inch and a half, in its two short axes, and two inches and a half in its long axis.
"A stone voided by a woman without being cut; given me by Dr. Massey." British Museum, 1809.

A c 27. Numerous small calculi, which with about two hundred others were removed from between the prepuce and glans penis of a very old man. The patient had congenital phimosis, the orifice of the prepuce scarcely admitting the introduction of a common probe. From the presence of the calculi the prepuce was distended to the size of a pullet's egg, and retention of urine was finally produced.
Presented by J. P. Vincent, Esq., 1842.

That the advice of the surgically great was not always what we would today consider wise, is recorded in specimen H49:

H 49. Several small calculi, presented by J. P. Vincent, Esq., with the following history, 1843:
Frederick Rule, aged 23 years, by occupated a boot-maker and who has generally had good health, was admitted into St. Bartholomew's Hospital under my care, Feb. 20, 1843, stating that he was suffering from incontinence of urine. On examining him, I found that to stop the constant flow of the urine, he was wearing a brass yoke; and that there was a tumour the size of a goose-egg in the perineal space just behind the scrotum. On handling this tumour, it gave the sensation of a collection of stones in a bag. The yoke was applied just behind the glans. On examining the urethra I found that a very narrow stricture existed about two inches from the orifice, below the usual situation in which the yoke was worn. Only the finest catgut could be passed through this stricture, and this came in contact with stones. The patient gave the following account: About ten years ago he was kicked by

a horse, when the parts about the pubis and the body of the penis were severely bruised; leeches, etc., were applied and he was unable to void his urine for forty-eight hours; when it began to flow, it was preceded by a coagulum of the figure of the urethra. About three weeks after this he had difficulty in making water, and afterwards it only dribbled away when the bladder was much distended. This incontinence of urine continued; and he was taken to Sir A. Cooper about twelve months after the accident from the horse, who recommended the yoke, which he has continued to wear up until this time. Six years ago he had bleeding from the urethra for several days, and he then perceived a swelling in the situation of the present tumour. This enlargement gradually increased to its present size; the incontinence continues, and he has now pain in the tumour when he is in exercise, etc. Feb. 25th, I made an incision into the most prominent part of the tumour, and gave exit to 146 calculi of various figures and sizes, the largest being about the size of a horse-bean. After the pouch had been emptied there were several in that part of the urethra next the bladder, which were removed, and two of the number came away the next day. The cyst consisted of a dense and tough membrane, like parchment. It communicated with the urethra its whole length and graduated into it, so as to offer no abrupt nor partial connection with it, and appearing to me to be formed by its dilatation. After the operation the patient retained his urine, passing it voluntarily through the wound.

Had I been asked the question, I believe I would have said that the knowledge and appreciation of calculus formation in the prostate gland was a recent development, and probably due to *x*-ray investigation. Not so. Here are three examples of several similar ones:

F 9. Numerous small calculi "from the prostate gland." Phosphate with a small quantity of carbonate of lime. Museum of Sir Astley Cooper, Bart.

H 55. A prostatic calculus removed by incision of the perineum from an agricultural laborer twenty-six years of age, by T. Herbert Barker, M.B. The man suffered from incontinence of urine since he was five years old; six days prior to the stone being removed a fistulous passage formed in the urethra, from which pus and a considerable quantity of urine escaped. When first examined he was labouring under complete retention of urine, and complained of considerable pain in the urethra and perineum; the penis was edematous, the perineum slightly swelled, and deep-seated hardness could be felt in its center, which gave the feeling of crepitation when moved from side to side. The presence of a stone could not be detected when a probe was passed into the fistulous opening. The patient recovered, and went to his work eight weeks after the operation; but neither at that time, nor subsequently, could he retain more than an ounce of urine in his bladder. This calculus is made up of 29 concretions closely adapted to each other by articulating surfaces.

H 13. One large and three small calculi, having articulating surfaces; these calculi were taken from the prostate gland, which was converted into a cyst: They consist of the mixed phosphates with a little urate of ammonia and carbonate of lime, and weigh 575 grains. One of these calculi protruded about one-tenth of an inch into the cavity of the bladder, through an ulcerated opening anterior to the natural opening of the urethra. That portion of the bladder and urethra which contained the calculi is preserved in spirit.
Presented by Wm. Lawrence, Esq., 1817.

The old lithotomists knew nothing of the types of calculi, thought nothing of the case histories, and added nothing to the knowledge of the etiology of calculus formation, but spent their time fighting over various and sundry methods, steps and tools of the operation. Hence we hear of the classical incision of Celsus, the lateral operation of Franco, the bilateral of Dupuytren, the perirectal of Nelaton, the mediobilateral of Civiale and the quadrilateral of Vidal de Cassis. There was the "*grand appareil*" and the "*petit appareil,*" merely a difference in the number of instruments the operator invented and used. What was, however, wanting in knowledge was supplied abundantly by speculation, for if we consult the works of medicine previous to the researches of Scheele, in 1776, we find them "filled with conjectures, which, however ingenious, were for the most part erroneous, generally absurd, and always founded on mere speculation."

As you know, Peter Franco, surgeon of Turrière, France, was the first to perform suprapubic lithotomy, in 1560, operating upon a child two years of age. Rosset, twenty years afterward, advised it; but not until three centuries after did John Douglas of England revive it and did it receive surgical recognition. The following is of interest:

B i 17. "Removed from the bladder of a boy 17 years of age, at St. George's Hospital, May 26, 1820. This was the first case of removal by the high operation without wounding the perineum; the boy soon recovered."
Presented by Sir E. Home, with the foregoing memorandum, 1820.

Likewise early attempts at lithotrity are of interest, and one of these procedures perfected in the hands of Civiale consisted of grasping the stone by means of a three-fingered "trilabe" and then with a centered drill the stone was perforated in an effort to effect either its rupture or to create a passage for urine.

B g 3. A calculus which was perforated by Mr. Costello at Bristol. The patient afterwards came to London and was admitted into St. Bartholomew's Hospital, where he died, previous to any further operation being attempted. The perforation remains, except that it is closed at both ends by the subsequent deposits.

Sir Everard Home mentions in his *Diseases of the Prostate*, the unique case of Colonel Martin, who attempted and is supposed to have succeeded in crushing a stone in his own bladder by means of a bougie with a serrated extremity.

H a 14. Portions of a brass pin which formed the nucleus of a urinary calculus, and to one of which the phosphates still adhere. The following particulars of the case were communicated by Anthony White, Esq.:

"Robert Cole, twenty-two years of age, had suffered from pains in the loins, bladder, and urethra for the last two years, during which time he had been treated for a supposed disease of the kidney. His urine was frequently tinged with blood, and he carried his body bent forwards, the upright position always producing an exaggeration of his symptoms. On examining the bladder with a sound, a large stone was felt, which was readily seized by the Lithotrity forceps, and measured twelve lines on the scale of the instrument. The stone was easily broken down by gentle blows with the hammer, but the smaller branch of the instrument could not by any means be brought in contact with the other branch, by nearly three lines and a half. On attempting to open the instrument, its branches were found to be so firmly fixed, that they resisted the most powerful efforts to separate them. The instrument was therefore withdrawn, in effecting which, however, the greatest difficulty was experienced; when the curved portion of the instrument had arrived at the neck of the bladder it remained fixed for a considerable time, but suddenly yielding, came with a violent jerk into the urethra, through which it was with difficulty drawn. The instrument being examined, its branches were found firmly wedged by two portions of the pin, which had been cut across. That portion of the pin on which the calculous matter still remains, was voided along with the urine on the following day. The patient stated that he had swallowed a pin five years before, but that he suffered no inconvenience from it until within the last two years, when he was attacked with pain in making water, etc. Notwithstanding the force which was required to withdraw the instrument, the patient did not evince any increase of pain during the operation, and he completely recovered without any bad symptoms."

Presented by Arthur White, Esq., 1842.

Nor was the "two-stage" operation unappreciated by the surgeons of the past century:

C 15. A compact oxalate of lime or mulberry calculus, presented by James Briggs, Esq., with the following history:

"Extraction from the bladder of a man aged 24 years, by trade a printer, at a second operation, affording one among others of the success of the method termed by the French 'Taille en deux temps.' In attempting to extract the stone during the first operation, it slipped from the forceps; and though it could be felt, it could not afterwards be laid hold of, in consequence of being apparently lodged in a pouch of the bladder. The operation was completed eight days afterwards, the stone being found in contact with the opening made into the bladder. It was necessary to enlarge the wound slightly, and its extraction was difficult; yet no ill consequence followed, either in the interval between the two operations or afterwards, and the recovery was more rapid than usual."

There are many calculi recorded that have particular interest because of their rarity and numerous others whose operations presented difficulties and unusual skill, but I will conclude with the citation of two whose quaint histories and graphic descriptions present very clearly the trials of the surgeons who worked in the days before modern advancements, and in themselves and their patients so ably portray their period in surgery.

We have all heard (and unfortunately still do hear) of the exploits of the unscrupulous claiming to be able to dissolve stone. Frequent references are found in the catalogue to the much-heralded values of "Friar's Balsam," "Constitution Water," and so forth; several mention the celebrated Mrs. Joanna Stephens, who finally succeeded in holding up Parliament itself for the neat sum of $30,000 before divulging the secret of her worthless remedy. The ingredients of this remedy were published in the *London Gazette* of June 19, 1739, and turned out to be a mixture of eggshells, garden snails, swines' cresses, soap and such vegetable ingredients as burdock seeds, hips and haws. In each one of her certified "cures" the stone was found in the bladder after death. But here let me present one of her disciples and let him tell his own story:

A 184. A small flat oval calculus taken after death from the bladder of William Hay, Esq., who took three ounces of Mrs. Stephens' medicine every day during five years, and for a considerable time afterwards a quantity of Castile soap, and also lime-water. Experience has fully confirmed the accuracy of Dr. Whytt's concluding remark, "that Mrs. Stephens' medicines, or soap and lime water, may give relief to patients, and make them pass through life, even although they have little effect in dissolving the stone." Mr. Hay continued taking this remedy to the last day of his life; he died of apoplexy in July 1775. By his own desire his body was opened, and the calculus contained in the bladder was placed in Sir Hans Sloane's collection, from which it was transferred to the College by Sir Joseph Banks.

Mr. Hay published a pamphlet, called an *Essay on Deformity*, at the end of which is a minute history of his own case and his opinion as to the efficacy of Mrs. Stephens' medicines, from which account the following has been taken:

"For many years red sand constantly came from me without pain or inconvenience. About nine years ago I began to be uneasy, and before twelve months had passed was so much out of order that I could no longer ride; the motion of a coach grew insupportable, and that of a chair or walking was generally attended with bloody water. I took Mrs. Stephens' medicines in the solid form, three ounces a day, for about five years, when I changed it for the same quantity of Castile soap, which about a year since I have reduced to two ounces and lately to one ounce with about a pint of lime-water mixed with milk, being willing to regain my liberty as far as is consistent with ease and safety. This regimen I have incessantly pursued, except some few days that I have purposely omitted it to observe the consequence of such omission. Whilst I pursue this regimen, I never discharge red sand, whenever I omit it for a few days I constantly do; by a steady perseverance in it my particular complaint has been gradually diminished and my health in general improved. I believe I could now ride, though I have not tried. I seldom feel any uneasiness in a coach, and when I do it is inconsiderable, though sometimes, though very rarely, it is attended with bloody water, and the motion of a chair or walking does not affect me. In short, I have exchanged pain for ease, and misery for comfort; and had it not been for this medicine, I should not have been alive to tell my story."

The calculus is mounted between glasses in a gold frame, on which is engraved: "this stone weighs 99 grains," and this is enclosed in a gold box. It was also accompanied by a manuscript on vellum in a gold-mounted shagreen case. British Museum.

The largest stone in the collection is accompanied by the following unusual history:

H 2. Calculus taken after death from the bladder of Sir Walter Ogilvie, Bart. It weighs forty-four ounces troy, and measures sixteen inches around its long axis, and fourteen inches around its short axis. This calculus was examined by Dr. Powell, and found to consist of the triple phosphate of ammonia and magnesia with phosphate of lime and a large quantity of animal matter. An account of this enormous and very characteristic specimen of the Fusible Calculus is given by Sir James Earle,[1] from which the following history has been abridged:

"Sir Walter Ogilvie, Bart., of Dundee, an officer in the regiment of Scotch Greys, at the age of twenty-three, active and healthy, was crossing the ferry at Leith when he received a blow on his back from the boom of the vessel, which paralyzed the pelvis and lower extremities. During two months he was obliged to have his water drawn off; for fourteen months he remained in bed, in a horizontal posture; and though he recovered the use of his bladder

[1] Earle, J.: Trans. Toy. Soc., London, 1809, p. 303.

and limbs sufficiently to walk across the room with the help of crutches, and also to ride, when placed on a low easy horse, his health continued many years in a weak and precarious state, while the limbs acquired little additional strength or power. About twenty years after the accident, perceiving symptoms of stone in the bladder, he was examined by Mr. Benjamin Bell of Edinburgh, and stone was felt, which was judged to have attained a considerable size; the operation of extraction was then recommended, but was postponed from time to time, though his health declined and the irritation and pains in his bladder gradually increased. Sir Walter continued to endure this state of existence twenty-eight years from the time of the accident, when he became unable to make water in an erect position: this inconvenience increased to such a degree that latterly he could make none without standing almost on his head, so as to cause the upper part of his bladder to become the lower, and this he was obliged to do frequently, sometimes every ten minutes, as the quantity voided each time was less than the measure of a wine-glass and when he used exercise, it was tinged with blood.

"These symptoms continued to increase in severity until the spasms and fits of pain from the urgent desire to void urine became so frequent and violent, and rendered his life so completely miserable, that he determined if possible, to have the stone extracted, and for that purpose came to London and placed himself under the care of Sir James Earle, it being then thirty years from the time of the accident. At this period the stone could be felt above the os pubis, forming a large prominent tumour, and on attempting to pass a sound, the instrument struck a solid mass which prevented its entering the bladder. Mr. Cline being called into consultation, it was determined that an attempt should be made to extract the stone by the lateral operation; in the hope that the calculus would be found sufficiently soft to admit of its being broken down, and thus taken away; its magnitude precluding any idea of its being removed in an entire state.

"Sir Walter being made perfectly aware of the difficulties to be apprehended in the extraction of the stone, and also of the uncertainty of the result, determined to submit to the operation, which Mr. Cline was requested to perform. The staff could be passed in no further than the neck of the bladder; the division of the urethra and prostate gland was made with the scalpel and probe-pointed bistoury: when this was accomplished, it was found impossible to introduce any kind of forceps; but on pressing hard with the finger, part of the stone felt soft, gave way, and made some room for the forceps, which brought away several portions, and with the assistance of a scoop as much stone was extracted as would have filled a large tea-cup; but the great mass beyond what the finger could reach on either side still remained hard and impenetrable, and after repeated trials with forceps of different kinds, and of the strongest powers, it was found impossible further to reduce the size of it, or take it away. The operation, which was necessarily protracted, was borne with great firmness; but the patient becoming much exhausted, it was judged right to relinquish any further endeavors to extract the stone. No hemorrhage ensued, he became calm and composed, and passed a tolerably good night; the next day he complained only of the same kind of spasms and frequent pressing desire to void urine that

he had been accustomed to feel, although they were not much more acute. On the third day from the operation peritonitis took place, which was subdued by bleeding and fomentation. From this time he appeared to improve in health and strength; his rest was, however, continually broken by repeated spasms, which kept him in a constant state of irritation, obliging him to violent efforts in resisting them, and to get instantly on his knees with his head low in the bed, to enable him to expel the urine, one spasm frequently succeeding before the former had well subsided. Towards the eighth day he was visibly growing weaker; his pulse smaller and quicker; his little inclination for food became less and he was with difficulty prevailed on to take any; some cordial medicines however revived him, but on the following day he grew impatient, feverish and restless, and on the tenth day after the operation, desiring not to be teased to take anything more, he covered himself completely with the bed-clothes, and quietly resigned his most singularly miserable existence."

Presented by Sir James Earle, 1808.

Gentlemen of the medical profession of the Twentieth Century, to us falls the duty to carry the torch, so nobly raised by these master surgeons of this elder day and to realize that they carried it to a pinnacle so high that its beams travelled the decades through and now it forms part of the ancestry to which we claim a heritage. It is delightful to marvel at their ability, to congratulate ourselves on being their lineal successors, heirs to their teaching, their vision in diagnosis, heirs to their splendid professional ethics and professional poise, yes, even heirs to their developed skill. Of all this we should be justly proud and justly zealous. But mind you, also, that there exists perhaps a closer relationship to these times, I might say even a blood relationship, and in your veins probably runs some of that vital, everlasting serum that flowed in the arteries of some of their patients, and when all is considered and carefully weighed, I do not know but that the heritage of that stamina which enabled them to stand with such fortitude the trials of the flesh of their day is perhaps the greater heritage of the two.

# SOME MEDICAL ASPECTS OF THE WRITINGS OF ÉMILE ZOLA*

By JOSEPH McFARLAND, M.D.

Responsibility for the remarks that follow rests upon the chairman of the Section and not upon the speaker. At a recent dinner, at which we were happily seated sided by side, conversation turned upon literature, then upon French literature, and finally upon the writings of Émile Zola. Before the table was cleared and the formal part of the occasion reached, in spite of my objection that this section dealt with medical history and not with literature, your chairman had my promise to present to you some informal reflections upon his writings.

Zola's writings are peculiarly rich in medical topics, as, indeed, in all things morbid; so true is it that one cannot help suspecting that the man himself was morbid. If not, he was certainly more than ordinarily curious about morbid states—physical, mental, moral, political and religious.

Most people are curious about the unusual, the horrible and the morbid. The crowds that gather about the scene of an accident evidently do so in the hope that they may catch a glimpse of a mangled corpse! Similar crowds, made up of persons who can ill afford the time, follow in the wake of arrests and police raids, throng magistrates' courts, sit through long trials and clamor for permits to view executions. The morgue, the dissecting-room, the surgical clinic, the anatomical and pathological museums, all have their quotas of morbidly interested visitors.

The sex plays a large part in the affairs of men, and a great part of literature is made up of descriptions of the courtships that precede the gratification of the passion. Its exaggerations and perversions constitute the themes of that forbidden salacious literature of which so little is said but of which so much is read.

Did Zola fill his books with the forbidden and the unusual because

* Read May 12, 1925.

he was himself morbidly curious, or did he shrewdly recognize the morbid cravings of other minds and deliberately set about gratifying them to his own profit? The sale records of his books suggest the latter; the more daringly he dealt with depravity the better the books sold and the more daring he became, until he transgressed every canon of decency.

Yet throughout his works there runs an evident desire to correct social abuses and improve the general welfare. He appears, or would appear, in the guise of a reformer, and his courageous conduct during the terrible Dreyfus affair, in which he placed himself in the position to be apprehended, tried and punished for his heroic defence of the friendless defendant, entitles him to the most careful consideration.

In a limited way there is a resemblance between the works of Charles Dickens and Émile Zola—each endeavors to point out some social evil in one of his books and to a certain extent each accomplished some good. Dickens' strictures upon the private schools and the debtors' prisons aroused the public to investigation and improvement; Zola's novel *L'Assomoir* (drink) has been declared to be the greatest temperance story ever written, and it did more than all the others to make his reputation.

But there are greater differences than resemblances. Dickens wrought magic by humorous exaggeration, characterization, and pathos; Zola attempted what he believed to be realistic presentations of human frailty in all its hideousness, unrelieved by any touch of humor. Dickens leaves his reader with a clear sense of the evil to be overcome and good hope of success in overcoming it; Zola leaves his reader with dismay in his heart. One reads Dickens and is thrilled and elevated; he reads Zola and is depressed and disgusted.

Émile Zola was born at Aix—the Plassans of the novels—April 2, 1840; he died, accidentally axphyxiated by gases from a defective flue, in Paris, September 29, 1902. Failing in his academic career, he began life for himself as a clerk, but began to write almost immediately, and in four years he gave up everything else and devoted himself to literature as a profession.

It would be interesting to learn where he acquired his medical knowledge, which is extensive, as he did not grow up in a medical environment and never was a medical student. But, as a matter of fact, his knowledge of medicine is no greater than that of law,

religion, politics and numerous other matters with which he deals in his books. It only strikes the reader as remarkable because it is less usual for a layman to know as much about medicine as about other subjects.

The book of greatest medical interest is, undoubtedly, *Lourdes;* but, as in it medicine is almost indissolubly mixed up with religion, I have thought it best, tonight, to devote my remarks to the series of books that Zola, no doubt, hoped to be his *chef d'ouvre*, the twenty volume series to which he gave the name *Les Rougon-Macquart*. All of these novels I have carefully read; only one, *La Rève*, would I care to read again.

They tell the story of a family of the Second Empire, with its collateral branches, running through three generations. The whole is imaginary, but is treated as though the people were real, and some of the same people appear in successive books with longer or shorter mention, accordingly as the story requires, until one becomes well acquainted with them.

Zola makes it appear as though the entire series was a scientific investigation of the problems of heredity, and brings that aspect to a focus in the last volume, *Docteur Pascal*, in which the hero is continually busy collecting, classifying, filing and connoting data obtained from every possible source referring to the various members of his family. Each item is filed in its appropriate "dossier," and each assigned member to his appropriate position on the family tree, of which a chart is introduced as a frontispiece to the volume.

In these stories more than twelve hundred characters appear, and the author compiled a bibliographical index in a separate volume for those desiring it.

And what a family to write about! The Rougon-Macquart are degenerates almost from beginning to end, and, although a few of them attain to wealth, to social position or enter the professions, not one of them conducts himself in an orderly, ethical, well-regulated manner. There is always some striking defect of character. French writers assume that every human being is obscessed by some ruling passion. Certainly every member of this family was, and these passions exaggerated by the prevailing degeneracy were frequently the causes of his undoing. Here is the beginning of the family and the source of its degeneracy:

Adelaide Fouquet, the mother of the family, was a neurotic, hysterical and cataleptic girl. She had as a husband Pierre Rougon,

a dull-witted, emaciated truck-gardener; then, as lover, Macquard, a drunkard and smuggler.

From the first alliance the legitimate branch of the family descended; from the second came a more numerous and more degenerate illegitimate branch. Macquard was shot by *gens d'arms*, after which the woman lived on until she reached the age of one hundred and five years, many of her last years being passed in an insane asylum in a state of total oblivion of all that went on about her. Her death from apoplexy occurred as her greatgrandson, Charles Saccard, a little hemophilic, while visiting her, was taken with a fatal nosebleed. Sitting directly in front of him, and seeing the blood gently trickle from his nose over his clothing until he fainted and died, she experienced an unexpected revival of memory, and fancied that she held in her arms a grandson, Silvère Mouret, who, having been shot as a smuggler by a *gen d'arm*, died in her lap. This was too much for her and she collapsed.

From these humble and defective beginnings the family descends. In its various ramifications are included individuals in all classes of society, from cabinet ministers, great merchants, rich bankers, ecclesiastics, doctors, manufacturers, to peasants and convicts. They suffer from a great variety of diseases—tuberculosis, gout, hydrocephalus, smallpox, locomotor ataxia, dementia, dropsy, anthracosis, hysteria, catalepsy, epilepsy, homicidal paranoia, apoplexy and dipsomania—all of which are attributed to heredity, or the excesses brought about by inherited vices. Curiously, though the works are supposed to be absolutely realistic, so far as I can remember there is no passage in which a venereal disease is hinted at: The locomotor ataxia from which Maxime suffered is said to be due to his "excesses." However, at the time at which Zola wrote, the relation of syphilis to tabes was not yet known.

The members of this family were guilty of every sin in the decalogue, and every crime in the legal catalogue—adultery, arson, assault, conspiracy, forgery, fornication, graft, missappropriation of trust funds, malfeasance in office, murder, prevarication, rape and seduction are but the worst, and the author seems to take keen delight in relating the crimes with vivid detail and in the grossest and coarsest manner. Indeed, the more a subject is taboo in social convention the more delight he seems to take in openly discussing it. The most unspeakable obscenities are sometimes described in revolting detail. Once launched upon such a theme, he knows no limits of language or description.

But the versatility of the writing is marvellous, and the variety of subjects covered remarkable. The series comprises the following:

*La Fortune des Rougon*, with which the whole begins.

*La Curcé*, which deals with political corruption and fraudulent real-estate transactions under the reign of Napoleon III.

*Le Ventre de Paris*, in which are described the food markets and manufactories of Paris.

*Le Conquêt de Plassans*. An account of ecclesiastical and political intrigue.

*Son Excellence Eugéne Rougon*, dealing with nepotism and political corruption.

*La Faute de l'Abbé Mouret*, dealing with Mariolatry in religion, and telling how it led the poor abbé astray and wrecked the life of a lovely girl.

*L'Assomoir*. The greatest temperance story every written.

*Une page d'Amour*.

*Nana*. The story of the most shameless of prostitutes.

*Pot Bouille*.

*Au Bonheur des Dames*. A wonderful account of the growth of a great department store.

*La Joiè de Vivre*.

*Germinal*. A wonderful account of the coal-mining industry with its strikes, shutdowns, sabbotage and the sufferings of the oppressed people.

*La Terre*. A story of peasant life, dealing especially with the peasants' love of the land. It is infamous and one of the most obscene books ever published.

*La Rève*. This is the only one of the series that may be called beautiful. It is free from objectional features, is full of beauties and is a rhapsody of beautiful embroidered church vestments, stained-glass windows, cathedral gardens, etc. Unfortunately, it is little read.

*Le Béte Humaine*. This deals with railroads, but also with murder and adultery on a grand scale.

*L'Argent*. A story of fraudulent stock speculation.

*La Debacle*. A great though horrible account of the battle of Sedan and the fall of Napoleon III.

*L'Ouvre*. This deals with art and artists.

*Le Docteur Pascal*, which finishes the series and gives Zola's conclusions. It purports to be scientific but ends otherwise.

In most of these books there are passages of great beauty and power: There are descriptions of landscapes, seascapes, sunrises, sunsets, storms and other natural phenomena that are fine. In some of the descriptions of the storms in *La Joiè de Vivre* one can almost feel the old house shake and hear the shutters rattle in the midst of the lightning and thunder. In *Le Béte Humaine* the account of the runaway train pounding along on its tracks, uncontrolled and gathering momentum as it goes, with fire coming

out of its smokestack and its terrified passengers awaiting the impending death, holds one breathless. The cool shades, the trickling waters, and the perfume of the flowers in the garden of Paradou in *La Faute de l'Abbé Mouret*, make that garden indeed an Eden. The description of the sun-kissed, freshly spread vegetables on the market stalls of Paris in *Le Ventre de Paris* fill one with wonder. The beautiful decorations of the *Bonheur des Dames* are visions of color and loveliness. The strike in *Germinal* is terrifying and the account of the final destruction of the mine appalling. The battle of Sedan in *La Debacle* is thrilling and grips the attention. The account of the snowstorm with which *La Rève* opens is beautiful, and the sufferings of the tiny child exposed to it pathetic in the extreme. But in general Zola's style is labored and tedious, very wordy and too much given to detail. The episodes—exciting, thrilling, terrifying or revolting—are too widely separated to sustain continued interest.

To enjoy the books—if enjoyment of such books be possible—they should be read in the order in which their names appear in the lists published in the front of each volume, which is the order in which I have mentioned them. However, if they cannot be so handled and one desires merely to sample them, I recommend two—*La Rève*, which is the most beautiful, and *La Terre*, which is the most horrible.

With so many medical subjects to draw from it is hard to choose. Most of his pictures are well drawn, but perhaps the most remarkable are the obstetrical cases, of which there are two: One, in *Pot Bouille*, in which the patient is a strong servant girl, who delivers herself. In order to save herself from the disgrace of an illegitimate child she wraps the baby in newspapers takes it out and deposits it upon a neighboring doorstep, then returns to bed, where she remains for a few days, suffering from "dysentery." The account of the coming on of the pains and the sequence of events would seem to be known only to one with more than casual knowledge of the subject and who had seen numerous labor cases. But more remarkable is the case of Louise Chanteau, in *La Joiè de Vivre*. She develops dystocia, suffers long and serious delay, after which a physician is called in to take the place of the midwife and finally succeeds in delivering her. Every detail is minutely described and it seems incredible that any one could have written it unless he had frequently stood at the bedside during actual accouchments. In graphic description and complete detail, it rivalled the famous

lectures of the late Prof. R. A. F. Penrose. But his science fails when it comes to the phenomenon of the spontaneous combustion of the human body. Dickens wrestled with it in *Bleak House* and the case of Crooks is well known; but Zola, in endeavoring to repeat the experiment, made "Uncle Macquart" die of spontaneous combustion that was not spontaneous, for in a drunken stupor the hot ashes from his pipe fell upon his trouserleg, igniting the cloth, then the flesh and so starting the fire that so completely consumed the old man that practically nothing at all remained.

Zola claimed that his writings were realistic. But to have been so they must have depicted real people, that did the real things that real people do. This they certainly did not do. He tells only of people that he created, and he made them do unnatural and hideously ugly and vicious things. To him men were only animals and he depicts only the animal nature, forgetting that most men bridle their baser passions. His characters gave free rein to their baser passions and, in consequence, became monsters of iniquity.

But supposing him to have been realistic. Supposing that there were or are such people, is it art to write about them? What is the purpose of art? We conceive it to be the creation of the beautiful for the purpose of elevating and ennobling the human mind. For that reason we dislike realism and admire the older romantic and idealistic school, for from its very beginnings the chief aim of literature has been to contrast ugliness with beauty, error with truth and vice with virtue, and, whether rightly or wrongly from the point of view of absolute truthfulness, make the latter triumph over the former. Under such circumstances the reader is left with his mental sense exalted, feeling that it does matter how one lives his life, and resolved to suppress his evil passions and show himself indeed a man.

But though many of Zola's characters are vicious beyond belief, nothing happens to them in consequence. They continue their evil lives until they pass from view toward the end of the volume. Scarcely any of his books have what might be called an ending. Perhaps that too is considered realistic, for, no matter what happens in real life, the world goes on just the same. But it is consistent with our old-fashioned view of literature to believe that a story should have an end. We want the hero to be triumphant; the villain to be dead; the circumstance to be finished and done, and we like to sigh with relief to think that it is so as we close the volume.

# THE BLACK DEATH—ITS SOCIAL AND ECONOMIC RESULTS*

By HERMAN B. ALLYN, M.D.

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The spectacle of a pestilence marching steadily on from East to West, claiming thousands of victims, unchecked by anything that man can do, inspires horror, and in proportion to the degree of ignorance and helplessness that prevails, an angry resentment, with the demand that something be done, even to the extent of human sacrifice. If in the story of the spread of the plague in the Middle Ages, with its processions, its futile worship of this god or its vain offerings at that shrine, its torture and wholesale slaughter of Jews, its burnings of suspected poisoners, we are appalled at the ignorant brutishness of mankind, let us remember that they were only just a little removed from paganism, and that even we have not yet, in our day, acquired in full measure the conviction that all men are brothers. Moreover, it is only within the memory of some of us that we have learned the causes and prevention of typhoid, of cholera, of typhus, of malarial fevers, of yellow fever and of plague.

Since more has been accomplished in the past fifty years by medical men in the discovery of the causes of disease and in their prevention than in all the previous centuries, it may be interesting historically to review the progress and consequences of the Black Death, which swept over Europe like a hurricane, causing many more deaths than the World War. We shall at least be the more thankful for living in the twentieth century.

Whether or not the plague that affected the Philistines after they had captured the Ark of the Covenant was bubonic plague affords a chance for an interesting discussion. You will recall that the men that did not die were smitten with the tumors. After they had suffered seven months of pestilence they were advised to send

* Read May 12, 1925.

the ark back with a trespass offering of five golden tumors and five golden mice, "images of your tumors and images of your mice that mar the land." The emerods (tumors) were evidently swellings that might easily have been buboes. After the Philistines had sent the ark back the pestilence abated among them, but seems to have attacked the Israelites, ostensibly because some of them profaned the ark by looking into it. It is certainly suspicious of bubonic plague that those who were attacked died very quickly: if they survived long enough to develop tumors recovery was possible.

As we shall see later, the pneumonic and septicemic forms are extremely fatal in from one to three days; if the victim lives four to seven days, buboes develop. It is quite probable that bubonic plague existed sporadically for many centuries. We know that there are endemic centers today in Yunnan, southern China; in Kurdistan; in southwestern Arabia; in central Africa (Uganda) and doubtless also in India, in central Asia and in Siberia. It is characteristic of all great epidemic diseases that they come in waves and then recede; that when they attack a virgin population the mortality is very great (for example, measles in the Faroë Islands); the same extreme fatality is noted when the disease recurs after an absence long enough to enable a new generation of susceptibles to be born and grow up.

Whatever opinion may be held as to the antiquity of the disease, W. Bulloch and Capt. S. R. Douglas are probably right in saying:

> The first historical notice of a disease like bubonic plague records its occurrence in Libya in the third century before Christ, or earlier; but this notice is only contained in a fragment from the writings of a much later physician, Rufus of Ephesus (about 100 A.D.), who also speaks of its occurrence in his own time in Libya, Egypt and Syria. Whether it was clearly known to the classical Greek writers on medicine is doubtful, but Aretaeus speaks of pestilential buboes. The plague of Athens described by Thucydides was apparently not this disease; nor was the destructive pestilence in the reign of Marcus Aurelius alluded to by Galen. We meet with bubonic plague again, however, in the great plague of Justinian, which started from Egypt, 542 A.D., and spread over a large part of Europe; it was described in Gaul as *lues inguinaria*. Epidemics succeeded one another in this and the succeeding century. At the end of the seventh century bubonic plague prevailed in Italy and is unmistakably recorded by Bede in England. But after that time it is difficult to follow the track of plague. Many European pestilences are spoken of in mediaeval histories which may or may not have been bubonic plague, though no sufficiently clear record remains.[1]

[1] Bullock, W., and Douglas, Capt. S. R.: Allbutt, Sir C., System of Medicine, London, 1912, ix, part ii, 358.

Classical and medical literature is full of references to the plague. The word signifies a stroke or blow, an allusion both to the suddenness as well as to the severity of the attack, particularly when the disease assumes epidemic form. While gradually the word plague has come to be limited specifically to bubonic plague, due to the Bacillus pestis, in earlier times it was applied loosely to a number of different diseases with the common characteristics of widespread distribution and great mortality. The best description of a plague in early times is that recorded by Thucydides, who writes of the plague in Athens in 430 B.C. Thucydides was himself attacked and he witnessed the sufferings of others. So vivid was the description given by this classic writer that it has influenced unduly the writings of many others, notably Boccaccio, who have not been content to describe objectively what they saw, but have been inclined to cast it in the phrases of Thucydides. There is some excuse for this, inasmuch as the disastrous effects upon a community of any great pestilence are much the same: fear, paralyzing effort and abolishing reason, justice, mercy and morality; heaps of dead with too few living to bury them; the survivors thinking only of their own pleasure and profit: "Eat, drink and be merry, for tomorrow we die" being their motto. Thucydides says:

The season was admitted to have been remarkably free from ordinary sickness; and if anybody was already ill of any other disease, it was absorbed in this. Many who were in perfect health, all in a moment, and without any apparent reason, were seized with violent heats in the head and with redness and inflammation of the eyes. Internally the throat and the tongue were quickly suffused with blood, and the breath became unnatural and fetid. There followed sneezing and hoarseness; in a short time the disorder, accompanied by a violent cough, reached the chest; then fastening lower down, it would move the stomach and bring on all the vomits of bile to which physicians have ever given names; and they were very distressing. An ineffectual retching producing violent straining attacked most of the sufferers; some as soon as the previous symptoms had abated, others not until long afterwards. The body externally was not so very hot to the touch, nor yet pale; it was of a livid colour inclining to red, and breaking out in pustules and ulcers. But the internal fever was intense: The sufferers could not bear to have on them even the finest linen garment. They insisted on being naked, and there was nothing which they longed for more eagerly than to throw themselves into cold water. And many of those who had no one to look after them actually plunged into cisterns, for they were tormented by increasing thirst, which was not in the least assuaged whether they drank little or much. They could not sleep: a restlessness which was intolerable never left them. While the disease was at its height the body,

instead of wasting away, held out amid these sufferings in a marvellous manner, and either they died on the seventh or ninth day, not of weakness, for their strength was not exhausted, but of internal fever, which was the end of most; or, if they survived, then the disease descended into the bowels and there produced violent ulceration; severe diarrhœa at the same time set in, and at a later stage caused exhaustion, which finally with few exceptions carried them off. For the disorder which had originally settled in the head passed gradually through the whole body, and, if a person got over the worst, would often seize the extremities and leave its mark, attacking the privy parts and the fingers and the toes; and some escaped with the loss of these, some with the loss of their eyes. Some again had no sooner recovered than they were seized with a forgetfulness of all things and knew neither themselves nor their friends.[1]

It seems to me noteworthy that Thucydides does not mention buboes in the plague at Athens. Yet buboes were well known at the time he wrote. In the second Book of the Epidemics it is said: "fever supervening on buboes is a bad sign except they be ephemeral, but buboes supervening on fever still worse." As Thucydides was a close observer, it is a fair inference that if buboes had been characteristic of the plague at Athens he would have mentioned them. Those who are interested in the nature of the pestilence at Athens will find it discussed by Raymond Crawfurd, M.A., M.D., F.R.C.P., in his book on *Plague and Pestilence in Literature and Art*.[2] Dr. Crawfurd thinks it was typhus, an opinion held also by Murchison.

There were a number of outbreaks of genuine bubonic plague, however, before the one that occurred in the fourteenth century, known as the Black Death, which particularly concerns us; and there were many pestilences in Italy and Rome which probably were not plague. They may have been typhus, malarial fever, typhoid, influenza or other diseases which occasionally assume epidemic form. Whenever they occurred there was the same panic, the same mob demand that something be done in the way of atoning sacrifice to placate angry or neglected gods. In the Middle Ages religious hatred added fury to ignorance. Crawfurd describes the persecution of the Jews in the following language:

Amid all the panic of the Black Death, persecution of the Jews broke out with even greater ferocity than during the Crusades in the twelfth century. Some victim was needed to appease the maddened populace: so the Jews

[1] Jowett's translation, quoted in Crawfurd, R., Plague and Pestilence in Literature and Art, Oxford, 1914.

[2] See previous note.

were accused of poisoning the wells, and even of infecting the air. Circumstantial accounts were circulated throughout Europe of secret operations directed from Toledo. The concoction of poisons from spiders, owls and other supposed venomous animals was described, and its mode of distribution made known. So well did their accusers deceive themselves that in many places the springs and wells were sealed, so that no one might use them, and the inhabitants of many cities had to rely on rain and river water. If confirmation of poison were ever needed, the rack could be trusted to procure it: or, failing that, men could be found vile enough to deposit poison in places in which circumstances demanded its presence. Those who escaped the fury of the mob fell into the clutches of an inexorable justice. In the case of the Jews the suspicion of poisoning was prompted by the fact that at this time the practice of medicine, at any rate in southern Europe, was chiefly in the hands of Jewish physicians. Hideous massacres of Jews had taken place in southern France and Spain in the previous epidemics of A.D. 1320 and 1333, as we know from the writings of Rabbi Joshua.

Many Christians also were accused of being poisoners. It became dangerous to touch a door or building with the fingers, lest a charge of poisoning be lodged against the suspected person, though no doubt he was as free from evil act as were the witches of Salem.

Hecker, in his *Epidemics of the Middle Ages*, gives the following account of what was reported of the plague in eastern countries before its arrival in Europe:

Cairo lost daily as many as ten to fifteen thousand, being as many as in modern times great plagues have carried off during their whole course. In China more than thirteen million are said to have died, and this is in correspondence with certain exaggerated accounts from the rest of Asia. India was depopulated. Tartary, Mesopotamia, Syria, Armenia were covered with dead bodies; the Kurds fled in vain to the mountains. In Caramania and Caesarea none were left alive. On the roads, in the camps, in the caravansaries unburied bodies were alone to be seen. In Aleppo five hundred died daily. Twenty-two thousand people and most of the animals were carried off in Gaza in six weeks. Cyprus lost almost all of its inhabitants, and ships without crews were often seen in the Mediterranean as afterward in the North Sea, driving about and spreading the plague wherever they went ashore.

Whatever confusion may exist as to the particular disease or diseases called plague and pestilence before and for some centuries after the Christian Era, by the Middle Ages we have a very clear picture of bubonic plague. It spread along the lanes of commerce

from China, India and Asia. Then as now the West highly prized the products of the East, especially spices, silks and gums. The merchandise was transported overland by caravan to Bagdad, or by ship through the Persian Gulf to the Tigris, thence up the Tigris to Bagdad; or to Ormuz on the Persian Gulf or to Aden at the entrance to the Red Sea, thence by boat and caravan to Koos on the Nile, or to Cairo, Pelusium or Alexandria. From Bagdad the route led over the plains of Mesopotamia to Lycia, the shortest route but the most dangerous on account of robbers. Another followed the Tigris up into Armenia, thence to Trebizond and other Black Sea ports, or taking the road from the Caspian upon the other side of the Caucasus which led to the Genoese and other Italian settlements in the Crimea. Some of you may need to be reminded that in the fourteenth century Italy controlled the commerce of the Mediterranean Sea, and that Genoa and Venice, through their great merchant princes, dominated all other cities in the control of the eastern trade. They brought untold wealth and prestige to their cities, and paid the price in introducing with their ships most devastating pestilences, among them the Black Death.

Gasquet says that in the countries along one of the trade routes by which the caravans reached the Italian ports in the Crimea, it is certain that the plague was raging with great virulence in 1346, the year before its arrival in Europe.

Gabriella de' Mussi, a notary of Piacenza, is the chief contemporary Italian authority upon the plague. He himself saw its outbreak in upper Italy. De' Mussi declares that Italian merchants had occupied Tana (Azov) and that in it they were besieged by Tartars and Saracens in 1346. The Italians were driven out of Tana and took refuge in Caffa, a Genoese settlement in the Crimea. The Tartars followed and laid seige to Caffa. The Death broke out in the Tartar host and thousands died daily. The Tartars threw the dead bodies of some of their own people over the walls with the hope of infecting the garrison. The garrison in turn cast the dead bodies into the sea, but nevertheless the city became infected and almost depopulated. Some of the survivors took ship and carried the disease with them to Genoa in 1347. Crawfurd says these ships seem to have infected Constantinople on the way. The Emperor Cantacuzenos, quoted by Crawfurd, notes the early low delirium, and distinguishes pneumonic, bubonic and carbuncular types of the disease. He mentions cervical and axillary but

not inguinal buboes, and also the dark patches on the skin that later came to be termed "tokens." Gasquet says that the special symptoms of the plague in 1348 and 1349 were four in number: First, gangrenous inflammation of the throat and lungs; second, violent pains in the region of the chest; third, the vomiting and spitting of blood, and fourth, the pestilential odor coming from the bodies and breath of the sick. The gangrenous inflammation of the throat might be explained by a tonsillar form of the disease, with secondary pyogenic infection such as causes the carbuncles which are sometimes present. The second form, with severe pains in the chest, no doubt indicates a pleuropneumonic type. The vomiting and spitting of blood indicates a severe type, septicemic or pneumonic. A contemporary writer says: "From the carbuncles and glandular swellings many recovered: from the blood spitting, none." Matteo Villani, writing of the plague at Florence, says that the sick who began to vomit blood quickly died. Guy de Chauliac says the epidemic was of two kinds: The first was marked by a "constant fever and blood spitting, and from this the patient died in three days." The second form was the well-known and less fatal bubonic type.[1] These quotations make it evident that the Black Death was bubonic plague; and that it showed itself at first in its pneumonic and septicemic forms. Those who survived long enough to have buboes sometimes recovered. Even in our own time, when the plague broke out in Manchuria, it presented itself in the pneumonic form, with a mortality of 100 per cent.

The adjective "black" as applied to disease, as "black" measles and "black" smallpox, probably means something more than a very severe type of the disease. I recall that the late Dr. Curtin told me that "black" measles was measles with pneumonia. Our own more recent experience with influenza of the severe type in which there were deep cyanosis, hemorrhages and pneumonia is illustrative. I have no doubt that the Black Death got its name because so many of its early victims showed cyanosis, petechial or other skin hemorrhages and pneumonia.

The symptoms of the pneumonic form are:

> The attack begins usually with one violent rigor, or repeated shivers, but these may be wanting. There are no prodomal symptoms. Headache, giddiness, vomiting, variable in intensity, follow. There is no primary bubo.

[1] Gasquet, F. A.: The Great Pestilence (A.D., 1348–1349) Now Commonly Known as the Black Death, London, 1893.

The facial expression is one of great anxiety and there is imperfect articulation as in the bubonic form. Pleuritic pain may be felt on the second, third or fourth day; cough, with expectoration, and râles heard on auscultation may commence on the third, fourth or fifth. The temperature is high, but does not differ especially from that in other forms of plague. The prominent symptoms are cough and blood-stained expectoration. Sometimes, but not always, marked haemoptysis and excessive dyspnoea with a tendency to cyanosis. The respiration rate, according to Müller, was as a rule over fifty, sometimes rising to seventy-five. The auscultatory signs are those of lobular pneumonia. The dulness on percussion is not marked. The sputa have no characteristic appearance, but are found to contain bacilli in enormous numbers. These are also detected in the blood. Swelling of the spleen is very marked. Death occurs from failure of the heart. In older accounts death is said to have occurred within two days. At Bombay about half the cases were fatal within five days, but some were prolonged to a week or more. The disease is almost invariably fatal. (Bulloch and Douglas.)

As stated, the "great mortality," as it was called, reached Genoa early in 1348, and soon afterward another ship or other ships carried it to Venice. At Genoa the plague spared hardly a seventh of the population. The mortality in Venice was about the same Gasquet says that out of twenty-four excellent doctors twenty died.

On Sunday March 30, 1348, the great council of Venice chose a commission of three to watch over the public safety. The rich fled from the place, officials could not be found and the great council was so reduced that the legal number for transacting business could not be gotten together. Notaries died in great numbers and the prisons were thrown open. When the epidemic had ceased the senate had great difficulty in finding three doctors for the city. In this emergency, Marco Leon, a capable physician and a native of Venice, who was in practice in Perugia, agreed to return to Venice. (Gasquet.)

Marco Leon seems to have had the necessary moral courage to stick to his job, dangerous though it was. In this respect his conduct stands in sharp contrast with that of Galen, who left Rome for Campania and later for Pergamus in the time of the pestilence brought from Syria by the army of Verus, A.D. 165, and with that of Galen's illustrious follower Sydenham, who abandoned London until the plague had subsided. In 1423 a pest-house or lazaretto was established in the island of Santa Maria di Nazaret. Forty days was the quarantine period, apparently because Christ spent forty days in the wilderness.

One of the earlier accounts of the plague is contained in the

introduction to the *Decameron* by Boccaccio. Boccaccio records that the plague visited Florence in the spring of 1348, spreading from the East where it had appeared several years before. He says that it did not appear in Florence as in the East, where if any bled at the nose it was a manifest sign of inevitable death, but that in men and women alike there appeared at the beginning of the malady certain swellings either on the groin or under the armpits, some as large as a common apple, others the size of an egg, which were vulgarly called plague-boils. From these two parts the buboes in a brief space appeared in every part of the body:

> Wherefrom after a while the fashion of the contagion began to change into black or livid blotches which showed themselves in many first on the arms and about the thighs, and afterward spread to every other part of the person, in some large and sparse, and in others small and thick sown; and like as the plague-boils had been first (and yet were) a very certain token of coming death, even so were these to every one to whom they came. Not only did few recover thereof but well-nigh all died within the third day after the appearance of the aforesaid signs: this sooner and that later and for the most part without fever or other accident.

He then records seeing two hogs mangling and attempting to eat the rags of a poor man who died of the plague. In a little while, after turning round and round as if they had taken poison, they fell down and died upon the rags.

> Thousands sickened daily, and being altogether unattended and unsuccored died well-nigh without recourse, some in open streets. The corpses were laid before the doors of the houses, where, especially in the morning, those who went about might see corpses without number. Between March and the following July what with the virulence of the pestilent sickness and the number of sick folk ill-tended or forsaken through the fearfulness of those who were whole, it is believed that upwards of an hundred thousand perished within the walls of the city of Florence.

The most important and particular account of the pestilence at Avignon is that of a certain canon of the Low Countries who wrote at the time from the city to a friend in Bruges. He was in the train of a cardinal on a visit to the Roman Curia when the plague broke out. He writes:

> The disease is three fold in its infection. That is to say, firstly, men suffer in their lungs and breathing, and whoever have these corrupted or even slightly attacked, cannot by any means escape or live beyond two days. Examinations have been made by doctors in many cities of Italy and also

in Avignon by order of the Pope in order to discover the origin of this disease. Many dead bodies have been thus opened and dissected and it is found that all who have died thus suddenly have had their lungs infected and have spat blood. [The first autopsies in plague that I know of.] There is another form of the sickness, however, at present running its course concurrently with the first; that is, certain aposthumes appear under both arms, and by these also people quickly die. A third form of the disease like the two former, running its course at this same time with them, is that from which people of both sexes suffer from aposthumes in the groin. This, likewise is quickly fatal. The disease has already grown to such proportions that no doctor will visit a sick man, even if the invalid would gladly give him everything he possessed; neither does a father visit his son, nor a mother her daughter, nor a brother his brother, nor a son his father, nor a friend his friend, nor an acquaintance his acquaintance, nor in fact does anyone visit another unless he is prepared to die with him or quickly follow after him . . . To put the matter shortly, a half or more than a half of the people at Avignon are already dead. Within the walls of the city there are now more than seven thousand houses shut up. In these no one is living, and all who have inhabited them are departed.

The canon also says that at Marseilles all the gates of the city with the exception of two small ones were closed, for there four-fifths of the inhabitants were dead.

Guy de Chauliac, in writing of the epidemic at Avignon, says:

The mortality commenced in the month of January, 1348, and lasted for the space of seven months. It was of two kinds: the first type lasted two months with constant fever and blood spitting, and with this people died within two days. The second lasted the rest of the time. In this, together with constant fever, there were external carbuncles or buboes under the arms or in the groin, and the disease ran its course in five days.

He goes on to say that the mortality was so great that it left hardly a fourth of the population. Even the doctors did not care to visit the sick from fear of infection, and when they did visit them they attempted nothing to heal them, and thus almost all those who were taken ill died, excepting toward the end of the epidemic when some few recovered. And then he adds: "As for me, to avoid infamy, I did not dare to absent myself, but still I was in continual fear." As a matter of fact, toward the end of the sickness, de Chauliac did take the infection and was in great danger for six weeks, but in the end recovered.

In 1348 the plague attacked England. In that year Calais was in the possession of the English. The islands of Jersey and Guernsey, with which England was in constant communication, were

decimated by the disease. Ships passing from Calais, in all probability, carried the plague to the seaports of England. Galfrid le Baker says that it first came to a seaport in Dorsetshire and then into the country, which it almost deprived of its inhabitants, and from thence it passed into Devon and Somerset to Bristol. It will be noticed that the plague was carried to Europe in ships, first from seaports in the Black Sea to Messina, Genoa and Venice, thence to Marseilles, and again, after sweeping through France, to England by way of Calais. Ships are notoriously full of rats and are by no means exempt from fleas (*Pulex cheopis* and *Ceratophyllus fasciatus*) and other vermin. There are vivid descriptions of ships the crews of which had all died of plague, drifting about in both the Mediterranean and the North Seas. When the ships struck land and were boarded by the inhabitants the plague broke out.

For the spread of the Black Death into and through England I have followed Gasquet, who, while not a physician but an abbot, has delved deeply into the original writings of the period, including the church records, the Patent Rolls on which are kept the grants and presentations to livings, and the *Inquisitiones post mortem* for the period of the plague.

It seems that the plague was brought from Calais to Melcombe Regis (Weymouth), a sea-coast town of Dorsetshire, either in the summer or autumn of 1348. Melcombe Regis was a town of considerable importance at this period, for during the siege of Calais by Edward III it furnished him with 20 ships and 264 mariners, while Bristol sent only 22 ships and 608 sailors, and even London sent only 25 ships and 662 men. The summer and autumn of 1348 were abnormally wet. It rained day or night with hardly an exception from June 24 to Christmas. I believe fleas thrive in dampness, so that the weather may have had something to do with the rapid spread of the plague. However that may be, the Black Death spread from Melcombe Regis, apparently first by waterways, to Bristol and rapidly throughout England. London is said by some to have been attacked as early as September 29, while others make the date as late as November 1. Fifty thousand are said by Stowe to have been buried in one churchyard. The narrow and dirty streets, the low unventilated and undrained houses, the lack of personal cleanliness, no rooms above ground, no soap or linen, living half the year on salt meats, all favored the rapid spread of the plague. Even in 1361, twenty-two years later, it

was the custom to kill cattle and hogs in the streets and cast the offal into the Thames, for in that year the king forbade it by letter. The exact loss of life caused by the Black Death in England cannot be determined. In fact there is no agreement as to the number of the population before the epidemic set in. Gasquet says it is placed at 4,000,000 or 5,000,000 by some, while Rogers thinks it could hardly be greater than 2,500,000, and probably was not more than 2,000,000. There is general agreement, however, that the Black Death carried off about half the population. Gasquet calculates that from the numbers of institutions some 5000 beneficed clergy died of plague. He adds that this number in reality represents only a portion of the clerical body, and that in any estimate of the whole, allowance must be made for chaplains, chantry priests, religious and others. "On this basis, and assuming the deaths of beneficed clergy to have been 5000, the total death-roll in the clerical order would be some 25,000."

The clergy seem to us to have been surprisingly numerous in England considering the population, and the same is true of its religious houses. Gasquet says that "in Nottinghamshire the proportion of deaths in the beneficed clergy is found, as in other cases, to be half of the total number. Out of 126 benefices in the county the incumbent died in 65 . . . In all, not including its 49 monasteries, the beneficed clergy of the county numbered some 700." If the nonbeneficed clergy were five times as numerous as the beneficed, this would make the figures for Nottinghamshire above 3500, not including the 49 monasteries. This was a heavy burden for the people and for the land to maintain.

Economic and Other Results of the Black Death. 1. The Black Death caused perhaps a greater loss of life than any pestilence before or since of which we have knowledge. It not only killed from a third to a half of the population of England, but it was equally fatal throughout the whole of Europe and what we now call the Near East. It was not so fatal in Germany as elsewhere, nevertheless the average mortality for the whole of Europe was not less than one-third, and it was probably nearer one-half the population. Such tremendous loss of life was bound to have noteworthy results on industry, on prices, on customs and on morals. Success, as Osler once said, is sometimes a question of survivorship. The man who survived the Black Death found himself, as laborers did during and after the World War, in a much better economic position.

We shall confine our statements to England because the researches of Gasquet and Rogers have supplied so much valuable information about this country. Before the plague there was a good harvest in England. At the time of the plague "there was sold a quarter of wheat for 12*d.*, a quarter of barley for 9*d.*, a quarter of beans for 8*d.*, a quarter of oats for 6*d.*, a large ox for 40*d.*, a good horse for six shillings, and even for 18*d.*" There was such a scarcity of laborers that none could be had for agricultural purposes. Twysden, quoted by Gasquet, says: "In the following autumn no one could get a harvester for less than 8*d.* with food. For this reason many crops perished in the fields . . . In one case where the owner of the property had died on July 28, 1349, it is said that 114 acres of pasture were let at 12*d.* per year, and 'not more this year because of the mortality and dearth of men.'" At Cliffe, apparently on property belonging to the deanery of Holderness, the rents of customary tenants and tenants at will are stated to have been usually worth ten pounds five shillings a year, but in this special year they had produced only two shillings. Prof. Thorold Rogers declares that everything that the landowner had to buy rose from 50 to 200 per cent. Iron, salt and clothing doubled in value. Herring, which formed an important part of the food of that generation, became so dear it was out of reach of the multitudes.

2. Since the Norman Conquest French had been not only the language spoken by the nobility and the clergy, but it had been, up to the fourteenth century, the language taught in the schools. This was not entirely a matter of choice, because instruction was almost exclusively in the hands of the clergy. Time and separation from France inevitably led to great corruption in the French in common use. You will recall that Chaucer says of the Prioress that she spoke French:

> After the scole of Stratford atte Bowe,
> For Frenche of Paris was to hire unknowe.

The successful war of Edward III against the French, the celebrated victories of Crécy and Poitiers, the capture of Calais, were possible because the national spirit of the English was back of the war. The English army was not an army of serfs and vassals. It was recruited largely from the yeomanry and was paid by the king. It was the clothyard shafts of the yeomanry, the shafts made famous in the stories of Robin Hood, which mowed down the French knights and their horses. So far as I know this was the first national army ever raised in England. When, therefore, the Black Death swept

away so many of the clergy and the teachers the times were ripe for a change in education. If the English could defeat the French in war, there was no reason why they should be dependent upon France for its language. Therefore when John Cornwall, described as a "maister of Gramer," who probably from his name was Cornish, began to teach English in the schools, his example was quickly followed; so that when Trevisa wrote, in 1385, he could say that in all the grammar schools of England the children "leveth Frensch, and construeth in Englisch." Thus the Black Death contributed not a little toward making the language of Chaucer and of Langland in *Piers Plowman* the language of the nation.

3. Farming at that time was under a manorial system, under the supervision of bailiffs, and the farmers practically, if not actually, serfs. They were not permitted to leave the land. The land was in common, the villeins supplying the tools and teams and perhaps the food when they worked the manor lands, as they did for the privilege of farming their strips. But, after the plague, laborers, as stated, were scarce. They would not farm the land unless paid wages. There were disputes as to what the wages should be. The king issued orders that laborers should work for the former wages; but the orders were not enforceable. If the church owners paid wages for their harvesting, it took sometimes more than they could obtain from the sale of the grain. If they did not pay wages, the grain was likely to rot uncut. In either case the churches were, in many instances, compelled to appeal to the king for remission of the sums due to him.

To be brief, a result of this struggle was gradually a change in land tenure, a leasing system giving place to the former bailiff system. Moreover, the commons were broken up into pieces by hedges to simplify farming. These hedges, I believe, are still to be seen.

In a more recent study of the Black Death on the estates of the See of Winchester, Miss A. Elizabeth Levett[1] maintains that there were no sudden or violent economic changes wrought by the Black Death. Changes in the labor service on the Episcopal manors had begun in 1208, but they were not yet complete in 1455. "No single manor in the Account Rolls had entirely commuted its labor services." Wages did increase, however, especially those of artizans and particularly those of the plumber. Perhaps the See of Winchester was more conservatively managed than other estates. The

[1] Levett, A. E.: Oxford Studies in Social and Legal History, Oxford, 1916, vol. v.

bishop may have been able to exercise greater control over his tenantry. It is reasonable to suppose, too, as Miss Levett indicates, that the plague was not as destructive in some parts of England as it was in others.

4. We have seen what a heavy toll was taken of the clergy, fully 50 per cent having died. One result was the difficulty of replacing them. The clergy behaved very much as the laborers did; they demanded higher salaries. Gasquet says that whereas before the pestilence, when there were plenty of priests, anyone could get a chaplain for five or even four marks, or for two marks and his board, after the plague there was hardly a soul who would accept a vicarage for twenty pounds. In the Winchester diocese, which he cites as an example, the average numer of priests ordained in each of the three years preceding 1349 was 111; in the fifteen subsequent years up to 1365, the yearly average was barely 20, and in the thirty-four years from 1367 to 1400, the annual average number of ordinations was only 27. The scarcity of men for the priesthood can be attributed in part to the great demand for the services of survivors to carry on the business of the nation.

5. The Universities of Oxford and Cambridge suffered the loss of thousands of students. "The celebrated Fitz Ralph, archbishop of Armagh, who had been Chancellor of the University before the event, declares that in his time of office there were 30,000 students at Oxford:[1] "So yt in my tyme, in ye University of Oxenford were thrilty thousand scolers at ones, and now beth unneth six thousand." In this statement he is borne out by Gascoigne, who, writing his *Theological Dictionary*, in the reign of Henry VI, says: "Before the great plague in England there were few quarrels between the people and few law cases, and so there were also few lawyers in the kingdom of England and few in Oxford, when there were 30,000 scholars at Oxford, as I have seen on the rolls of the ancient Chancellors, when I was Chancellor there."[2]

The editor says on the passage:

> They, *i. e.*, the students, came from all parts of Europe. The number seems incredible, but Oxfordshire was, to judge from its rating for exceptional taxation, after Norfolk, then at the best of its industries, the wealthiest county in England by a considerable proportion. . . . This concourse of students was diverted by the great plague. . . . I see no

[1] Harl Ms., 1900, vol. ii: Treaisa's Translation of Fitz Ralph's Propositio Coram Papa.

[2] Gascoigne: Loci ex Libro Veritatum, Ed. J. E. Thorold Rogers, p. 202.

reason to doubt the statement about the exceeding populousness of Oxford in the first half of the 14th century. (Gasquet.)

The king was so disturbed by the great falling-off that he addressed a letter to the bishops on the subject, urging that the clerical order be increased in number, morals and knowledge.

6. It is the general testimony of most observers that the effect of the Black Death was, as we have found war to be, destructive of moral and religious restraints. Instead, as some might think, that imminence of death makes a man walk in the fear of God, in the presence of plague he fears his own fears, but neither God, man nor devil; he becomes brutish and licentious. In England, and probably the same was true on the Continent, the young, inexperienced clergy who had to be appointed to replace those who had died from plague, naturally exercised very little restraining influence on the people.

As the combined result of the low state of intelligence and morals, of the inability of the clergy to inspire confidence in their spiritual leadership, of the prevailing conviction that supplication to God, or the intercession of some saint (Sebastian or Rocco were the most popular) would avert the plague, there developed societies based upon the idea that mortifying the flesh by the penance of public scourging would appease offended deity and avert the plague. Thus during the Middle Ages the "Flagellants" in great numbers marched through the cities, singing dirges and beating themselves with cords. Sometimes they took possession of a city, to the great disturbance of peace, order and quiet. They became such a nuisance even to the regular clergy that finally they were forbidden by the pope.[1]

The helplessness of the medical profession in the presence of plague and the extent to which even the more intelligent of them were dominated by current superstitions of the time may be judged by the advice of Guy de Chauliac. According to Raymond Crawfurd, among other preservatives he reckoned venesection, purification of the air by means of fires, comforting the heart with treacle and apples and things of savory flavor, consoling the humors with Galen's Armenian bole, and the prevention of putrefaction by the use of bitter things. Should the disease defy all these precautions, he then commends, as curative measures, bleedings and evacuations, with electuaries and cordial syrups. Buboes should be ripened with poultices of figs and boiled onions, pounded and mixed with

[1] Crawfurd, R.: Op. cit., p. 104.

leaven and butter. Then they should be opened and treated like ulcers.[1]

Ambroise Paré, at a later date, was not above the unworthy suspicions of his time. He writes:

> What shall I add? They must keep an eye on certain thieves, murderers, poisoners, worse than inhuman, who grease and smear the walls and doors of rich houses with matter from buboes and carbuncles and other excretions of the plague-stricken, so as to infect the houses and thus be enabled to break into them, pillage and strip them, and even strangle the poor sick in their beds: which was done at Lyons in the year 1565. God! What punishment such fellows deserve: but this I leave to the discretion of the magistrates, who have charge of such duties.

Paré recommends the wearing of an amulet of arsenic over the heart in order that "the heart might become accustomed to poison, and so be the less innured when other poisons sought it."[2]

Though good does not arise out of evil, the very magnitude of the evil does sometimes inspire men of common sense and human sympathy to the establishment of an institution of recognized helpfulness. To the plague in Florence, 1244 A.D., we owe the founding of the first ambulance society in Europe, the Campagnia della Miseracordia. It is curious and amusing to read that the money for the purpose was acquired through the fines paid by woolsorters for the use of foul and blasphemous language at their meeting-house. One of their number, Piero di Luca Borsi, induced them, when the fines had reached a large sum, to spend the money in the purchase of six litters, one for each ward of the city, and to select two of their members weekly for each litter to carry sick persons to the hospitals or dead bodies to their burial. I have heard that the society is still in existence.

Anyone who is interested in the effect of the plague upon art should consult Raymond Crawfurd's interesting book. It is surprising how many great artists have painted plague scenes, or have portrayed St. Sebastian or St. Rocco, the patron saints of plague.

As to the effect of the Black Death on architecture I am not competent to speak, but those who have studied the subject seem to agree that building was almost stopped for a while, and that where it was resumed after interruption there can be traced a replacing of the figured and ornate style by the perpendicular.

[1] Crawfurd, R.: Op. cit., p. 121.
[2] Paré, A.: Livre de la Peste, quoted by Crawfurd, R., op. cit., p. 158.

# JEAN MARTIN CHARCOT*

By WILLIAM G. SPILLER, M.D.

Jean Martin Charcot was born in Paris, November 29, 1825. His father was a carriage-builder; but, recognizing that his son, Jean, gave promise of great things, he bestowed upon him a better education than he himself had received. Jean hesitated in his choice between the pursuit of art and that of medicine, and finally selected the latter, although his artistic tastes were never buried and proved to be of value to him in his medical life. He was always the artist. The following anecdote has been told concerning the Charcot family. The father called his boys about him and said: "You are all old enough to choose professions. My means are not sufficient for further education of you all, although they will allow me to give advantages to one of you. I have determined that you, Martin, shall be a carriage-builder as I am. You, Émile, will enter the army, and your brother Eugene will be a sailor. As for you, Jean, as you have much ability in drawing, you may be a painter, if you wish; but as you are diligent you may complete your studies and become a physician."

It appears that the four sons followed the determination of the father, with possibly the exception of the one destined to be a sailor. This one seems to have gone with a regiment to Africa and his fate was unknown. His adventuresome spirit seems to have been inherited by his nephew, the son of Jean Martin Charcot, for the young Jean B. Charcot began his professional life as a physician, and, after giving some indication of following in his father's footsteps as a neurologist, was lured away by his love of travel and gained fame as an explorer in the Antarctic regions.

In 1848, when twenty-three years of age, Charcot became intern in the hospitals of Paris, and served one year at the Salpêtrière, a hospital which later was to owe its chief glory to the learning and enterprise of this man. He graduated in medicine in 1853. From

* Read October 13, 1925.

1853 to 1855 he was chief of the medical clinic, and in 1862 he was a member of the medical faculty of Paris and became physician to the Salpêtrière. His medical career thus began and ended in the Paris almshouse for old women, a place in some respects resembling our own Philadelphia General Hospital as it has been in the past. He was not confined to the study of women, however, for a division for men was established for him.

Charcot had the power of observation in a degree few men possess. One of his favorite sayings was to the effect that we see especially those things we have been once taught to see. The truth of this cannot be disputed. Much of importance is overlooked until someone with exceptional eye detects the unrecognized. Charcot's method combined the clinical with the pathological, and he was one of the earliest investigators in medicine to carry this fruitful study to great development. It has become so common now and its results have been so clarifying that we have difficulty in realizing that it was not always a means of study carried to its limits. He was, therefore, at first a student chiefly of organic medicine, but in the later years of his life his attention was attracted by the functional disturbances of the nervous system.

Fom 1872 to 1881 Charcot was professor of pathology, and he gave lectures on diseases of the different viscera of the human body. His work on the disorders of the lungs, liver and kidneys was highly esteemed and even at this late date is considered by pathologists as of exceptional value. His fame rests, however, chiefly on his studies of the nervous system.

The French system sometimes works in a very peculiar manner. When a vacancy occurs the man who stands in the line of promotion is likely to obtain the chair, whether his previous life has especially fitted him for it or not. Thus Dejerine, who had always been known only as a neurologist, had for a time the chair of pathology until he succeeded to the chair previously filled by Charcot. Letulle, who was known as a pathologist, filled the chair for the history of medicine. Pierre Marie also occupied the chair of pathology until the death of Dejerine left vacant the chair of neurology, to which Marie was called. At the present time, Roussy, whose work has been chiefly that of a neurologist, has very recently been made professor of pathology.

In 1882 the professorship of neurology was created especially for Charcot, and from this time dates the fame of the Salpêtrière as the

greatest neurological hospital in the world. At the time of Charcot's death the Salpêtrière received this tribute from Erb. He said that from no other place had originated such a group of prominent neurologists. Charcot's pupils embraced the names of Bouchard, Cornil, Ball, Debove, Raymond, Lépine, Hanot, Joffroy, Gombault, Cotard, Magnan, Pierret, Féré, Ballet, Gilles de la Tourette, Brissaud, Pitres, Richer, Babinski, Hallion, Souques and Marie. It is noteworthy that, with one exception, every young French neurologist living at the time of Charcot was his pupil and called him maître. Dejerine was the exception and gave the name of maître to Vulpian, who was a colleague of Charcot.

The fame of Charcot drew men from every civilized nation to Paris, and his lecture-room, which was very large, was always crowded, and not merely by medical men. This room was peculiar as was almost everything relating to Charcot. I have been often in it. It was of considerable length and rather narrow for its length. The floor descended gradually from the back toward the platform, which extended across the entire width of the lecture-room and was raised a few feet above the floor. This platform was sufficiently large to accommodate, I suppose, from twenty-five to fifty persons, who occupied it during a lecture by Charcot. These were Charcot, his assistants, French and foreign physicians, scientists, and the patients.

Charcot was not considered a great orator; his method of speech was direct and clear, and his presentation of a case all that one could desire. He would pass from patient to patient during his lectures to illustrate some feature he wished to make clear; would at times imitate some condition he wished to demonstrate to his hearers.

He lectured twice weekly. The Tuesday meetings, the famous Leçons du Mardi, were presentations of the most interesting nervous cases that were to be found in the outpatient department and possibly also in the wards; but the Friday discourse was a carefully prepared paper that was always worthy of publication in a medical journal of the highest rank. These Friday lectures were the supreme effort of his life; frequently he occupied an entire week in the preparation of a single lecture, and when interested in a particular subject he was known to employ a part of his vacation in the preparation for his lectures. His method was followed by his successor, Raymond, whose Friday lectures also were efforts indicative of

great research and observation. I often had the delight of listening to them, and on one occasion while I was in Paris studying at the Salpêtrière a distinguished visiting German neurologist remarked to me that there were no lectures for students in Paris, but only for physicians. It has always been a source of the deepest regret to me that I lost the opportunity of hearing Charcot lecture. I was studying in Vienna at the time of his death and did not reach Paris until a little more than a year later.

Charcot has been likened in his appearance to a Roman senator, to a Cesar or to Napoleon, and he was a man of exceptional dignity and reserve.

It is hard to grasp the development of medicine at the time Charcot began his studies and to appreciate what he actually accomplished, as so much of it has become common knowledge. Almost nothing was known concerning cerebral localization. Fritsch, Hitzig and Ferrier had not done their work, and the view of Flourens, that the cerebrum is a homogeneous mass and that symptoms result proportional to the amount of brain tissue destroyed, received the sanction of scientists. Broca's discovery of the localization of the motor speech-center was made in 1863, although the value of this localization was later called in question by a pupil of Broca, Pierre Marie. The discovery of the excitability of the cerebral cortex to electricity was of the greatest aid in the study of cerebral localization, although at first it was accepted with much skepticism, and yet it was the method employed by Grünbaum and Sherrington in their remarkable study on the gorilla. Charcot was among the earliest to properly evaluate cerebral localization. The subject has become so well known now that we have difficulty in recognizing that brain surgery depends on this discovery, and that the subject ever was one for controversy. Among his most distinguished opponents was Brown Séquard, at one time professor at Harvard, who offered the results obtained by himself as contradictory to Charcot's teaching.

Charcot's earlier work was devoted to the disorders of old age, for which the Salpêtrière afforded abundant material. To this period belong his valuable investigations on hemorrhage and softening of the brain. He studied tremor in its various forms and made the recognition of Parkinson's disease common property, for in 1868 the diagnosis of a case of this now well-known disorder was considered a brilliant achievement. At this time Duchenne, of Boulogne, was

beginning the recognition of tabes, but his ideas of its pathology would not be accepted at the present day. To Charcot pathology had ever been of vast importance, and even when professor of this subject he lectured and worked with unusual interest on the pathology of the nervous system.

Although it was Türck who first described secondary degeneration, it was Charcot who showed that degeneration of motor tracts would result from a lesion of the spinal cord or motor cortex of the brain, as truly as from a lesion of the internal capsule, mentioned by Türck. It was Charcot who first taught the trophic influence of the motor cells of the anterior horns of the spinal cord and pointed out the important relation of these cells in anterior poliomyelitis. He taught the recognition of pseudobulbar paralysis.

Sclerotic plaques were recognized as necropsic findings before the time of Charcot, but it was he who first taught how to evaluate the symptoms of multiple sclerosis and to make the clinical diagnosis of it possible. The close relationship of syphilis to so many disorders of the nervous system, as we now acknowledge, was unknown at the period of Charcot's life; but he recognized that Jacksonian epilepsy may be caused by syphilis and he obtained cures with mercury. He made no claims as being the first to recognize this form of epilepsy, but gave the credit, where it belonged, to Hughlings Jackson. He devoted much attention to the symptoms produced by lesions of the internal capsule. He added much to the study of tabes, and his discovery of the tabetic arthropathies led to the classifying of these deformities as Charcot's disease, a term which led to some confusion as it has been employed for an entirely different affection. These defects are still known as Charcot joints. The nature of these disorders was at first combated vigorously, but they have finally been recognized as trophic disorders. Charcot was invited to lecture in London. He did so and presented certain specimens of arthropathy to the museums of that city. He, with Erb, recognized primary lateral sclerosis, which likewise was the subject of acrimonious discussion. To him alone is due all honor for his discovery of that terrible disease, amyotrophic lateral sclerosis, which he described so fully that Marie likened his description to the birth of the goddess fully equipped from the head of Jupiter. Charcot himself regretted that his name was attached to so terrible a disease, one always fatal. At the celebration of the centenary of Charcot's birth this disease and migraine were chosen as the subjects for special

discussion, as both had received much attention from Charcot. He showed, in 1859, that intermittent claudication was caused by ischemia. This peculiar affection, which many years later was called by Erb intermittent lameness, was still almost unrecognized by the medical profession thirty years after Charcot first called attention to it, and indeed, it was not until Erb made it the subject of a monograph that it began to excite widespread interest. It would be difficult, nay impossible, to do justice to all the disorders described by Charcot. Erb, in the magnificent tribute paid to him shortly after his death, said there was scarcely a disease of the nervous system which was not studied by Charcot, and of every one the knowledge was advanced by his study. It is striking that his early studies were almost entirely on organic neurology.

In 1870 a department for epilepsy and hysteria was placed under his care, and from this event dates those famous studies on hysteria and hypnotism. At times a cloud has seemed to drift over his work on these subjects. It has been said that many of his patients were unconsciously educated by suggestion from physicians and other patients, and that hysteria as seen at the Salpêtrière did not exist elsewhere. Indeed, so much was classed under hysteria that Babinski finally found it necessary to cleanse the Augean stables, and asserted that not sufficient credit had been given to the effect of suggestion and involuntary education, and Marie, while acknowledging this, gave credit to Charcot for much that he had done in the study of hysteria. It was recognized in the World War that hysteria was of vast importance and that much still was due to Charcot's investigations, especially the hysteria of males and that associated with trauma.

Charcot was very active until his sudden death at the age of sixty-seven years. He died August 16, 1893. It was fitting that the most distinguished living German neurologist, Erb, should write an obituary notice. It is all the more noteworthy as at this time there was still much bitterness between the French and Germans resulting from the Franco-German War; but Erb acknowledged that Charcot had always treated German physicians cordially when they visited him, as many did, among these Frankl-Hochwart and Freud. Erb wrote: "A few weeks ago the surprising and distressing news came to us from France: Charcot is dead. He died suddenly from an attack of angina pectoris, far from his family, in the arms of two of his pupils and friends, while he was on a journey for

pleasure. The brightest star in the medical firmament of France has faded; Paris and all France have suffered a heavy, an irreparable loss, which is so much greater because it was entirely unexpected."

It is interesting to give a little consideration to the hospital where Charcot began and ended his work. The name Salpêtrière refers to saltpeter, which at one time was manufactured on the site of the hospital. The grounds of the hospital are extensive and the buildings very old. The beds for the patients, when I was familiar with the institution, were old-fashioned and stood high from the floor, and about some of them were curtains which could be readily drawn, and in this way seclusion could be obtained, so much employed by Dejerine in the treatment of neurotic cases. The nurses were inferior to those of our hospitals; they were not trained nurses as we understand the term. What the present condition of the nursing is I am unable to say. Many of the buildings belonging to this hospital group were low, about two stories high. They were made of stone. The Philadelphia General Hospital, which is to be destroyed, is a palace in comparison with the Salpêtrière. The grounds of the Salpêtrière were attractive, and the buildings gave more open space than do the buildings of our city hospital, but the two hospitals are similar in their number of beds. A recent history of this ancient hospital has been placed on the market by the present incumbent of the chair of neurology, Georges Guillain, written with P. Mathieu.

Some years ago, possibly twenty, I had the pleasure of showing Guillain, now Charcot's successor in the chair of neurology, through the wards of the Philadelphia General Hospital. Dr. Shoemaker was then Director of Health and was at that time working for the destruction of the old buildings and the erection of a new hospital. Guillain had some difficulty in accepting my statements when I told him of this proposed change.

# THE SURGICAL TREATMENT OF PULMONARY TUBERCULOSIS*

## The Mütter Lecture

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It is with no ordinary pleasure that I appear tonight before a body of Philadelphia physicians, for there are close bonds uniting us. Sentiment is the great force in this world and even the callous surgeon feels its influence. I am a son of McGill, of Montreal; and Montreal and Philadelphia make a common boast, that of possessing two of the oldest medical schools in this continent. An old medical school means a "tradition;" a tradition of learning. And that is a great bond between universities. There is also the more individual bond of personal friendship. Many good friends of mine and yours are Philadelphians; and some good friends of yours and mine, called to be members of your universities, are Canadians. So that the great honor of delivering this year's Mütter lecture becomes a double pleasure.

Your secretary, Dr. Müller, suggested that I should take as my subject the surgical treatment of certain forms of pulmonary tuberculosis. I do this gladly, not only because this problem has been for the last dozen years of quite particular interest to me personally, but also because it has certainly a great future and is still insufficiently recognized in this continent.

A surgical operation such as that of total extrapleural thoracoplasty for unilateral pulmonary tuberculosis, not many years ago, was regarded by most internists as a piece of folly, not untinged by knavery. Things are different now. The courage of the pioneer has once again justified itself, for it was based on sound pathology and physiology. Sauerbruch has operated on over 700 cases and

* Read, December 11, 1925.

his work is everywhere accepted. Alexander's recent book, awarded the Quinquennial Samuel D. Gross Prize for 1925, by the Philadelphia Academy of Surgery, a monument for all time commemorating not only a piece of most valuable work but also the indomitable courage and industry of one who labored under an extraordinary handicap, embraces a critical analysis of five hundred articles upon the subject of the surgery of pulmonary tuberculosis and is a record of the very rapid widening of this field within the last ten or fifteen years. The bulk of the work hitherto we owe to Germany, Switzerland and Austria. Yet we, on this side of the water, have recently "caught on." Enthusiasm is spreading rapidly, in some cases too rapidly perhaps for discretion; and I think I perceive in this particular field of therapeutics the imminence of a danger which is apt to attend any new operative procedure—eagerness untempered by judgment, a very human impulse of pity uncorrected by knowledge, enthusiasm which regards not caution.

In this idea I have thought it worth while to devote the major portion of this lecture to a consideration of the general pathological aspects of pulmonary tuberculosis in the light of their application to the selection of patients for operation.

Let me, by way of introduction, say a few words of a general nature.

The operation in question is now more or less standardized. Its accepted title is extrapleural thoracoplasty. It consists in a resection of several inches of all the ribs of one side posteriorly, from the first to the eleventh, a resection which keeps outside the parietal pleura. That side of the chest wall consequently falls in, and the inward spring of the rib stumps compresses the lung, which also of its own motion collapses, to a certain extent, by reason of its elastic structure, in so far as that is preserved. Respiratory movements, dependent as they are upon rib movements, cease in great part, and the lung is given physiological rest. Such is the reason of the operation, and such is also the basis of ancillary operations—phrenicotomy to paralyze the diaphragm; the cutting of pleural band-adhesions which restrain the lung collapse of an otherwise good pneumothorax; the "plombierung" operations with apicolysis designed to compress strictly localized cavities in the upper lobe. All these I leave out of the discussion in this place. Nor can I take up, unless very briefly, other variants of the surgical problem, such as the place of thoracoplasty as opposed to artificial pneumthorax, total

or partial; partial thoracoplasties for limited disease; partial thoracoplasty combined with partial pneumothorax; the treatment of pyopneumothorax, with or without bronchial fistula; and other minor particularities. The subject then is here confined to uncomplicated chronic pulmonary phthisis, usually with cavitation, as seen in later adolescence and in adults, for which the standard extrapleural thoracoplasty is now generally accepted as not only a justifiable but a very gratifying procedure in selected cases.

All sound therapy, surgical as well as medical, rests upon a pathological basis. Before we can presume to do such a serious thing as an extensive operation upon such frail material as is represented by the far advanced tuberculous patient, it is our duty to be familiar with the pathology of the tuberculous lung, as well as with the clinical course of the disease. Fundamentally the extent of the disease, its type, and its mode of progression, depend upon the interaction of two opposing forces, the organism in its varying degrees of virulence, on the one hand, and on the other the defensive power, or resistance, of the host. The resultant effect represents the pathological condition of the lung at any given moment. But it is not only this that we have to estimate. In the endeavor to form a judgment upon the advisability of surgical interference in the patient as he comes to us for an opinion, we must look both backward and forward. We must ask ourselves, what has been the clinical course of the disease hitherto; what measure of the ordinary hygienic treatment has he enjoyed; what evidence has he given of resistance; and for the future, what is likely to become of him should no operation be attempted?

The Pathological Aspects in the Uncompressed and the Compressed Lung. It would seem that the pathological classification, which has been so well worked out by the Germans, particularly by Ranke, by Fraënkel and Albrecht, by Aschoff and Nicol, into two main types, the exudative and the productive, is applicable to clinical work in a most advantageous way. The histological reaction in the exudative form, which is always a more or less acute process, consists in the collection of a fibrin-containing fluid in the lung parenchyma, together with the usual cell elements, represented by lymphocytes, polynuclears, red cells, and cells exfoliated from the alveolar walls. The amount of fluid thrown out, in and around the foci of bacillary irritation, approximates the condition to that of lobular, or even lobar pneumonia. And when one considers the

fate of such a tuberculous exudate, one must keep in mind, as has been convincingly demonstrated by the *x*-ray work of recent years, that resorption of the exudate, within the space even of a few months, may be almost complete. An acute exudative tuberculosis may disappear almost like an ordinary lobar pneumonia. Yet such, of course, is not the usual result. Caseation begins in the middle of the cell exudate, progresses, and involves the alveolar wall and the surrounding lung parenchyma with the stroma. A restoration to normal is then impossible. Failing further progression, the caseous focus, with its surrounding granulation tissue, may dry up, and may be turned into scar with a surrounding ring, or capsule, of fibrous and hyaline tissue, in which calcification may ultimately appear. Or, on the other hand, the caseous focus may break down and the end-result is cavity. If resistance is strong, this exudative acute form may turn into the chronic productive type. If not, it goes on to bronchopneumonia or pneumonic phthisis.

The productive form is characterized by a relative absence of fluid exudate. It leads rather to the formation of the typical tubercle and tuberculous granulation tissue, such as we are accustomed to see depicted in our student textbooks. The tubercle, in its early stages, is composed of endothelioid cells, which in places fuse and form giant cells; these are surrounded by lymphocytes, alveolar cells, and proliferated cells from the stroma and vessel walls. The number of giant cells, the relative isolation of the tubercle, and the lack of surrounding fluid exudate are considered as a measure of the productive type of reaction. Such a tubercle is apt to destroy the tissue of the host more or less completely, in its own microscopic field, and in particular the elastic fibers. A *restitutio ad integrum* is impossible; but, in revenge, the defensive forces of the host play here a stronger rôle than is usual in the acute exudative form. While caseation of the center of the tubercle, with sloughing out, expectoration, and the formation of small cavities, frequently occurs, it is perhaps no less frequent to observe a hyaline and fibrous transformation of the whole tubercle into a solid scar; or at least the formation of a dense, fibrous capsule around a minute, inert, caseous mass. The exudative form is generally held to represent an acute process, and to be the result of a massive or highly virulent infection; the productive type to be the result of infection by a few bacilli, to which is opposed a strong defence.

In general the latter tends toward healing, the former toward breaking down. The one is nodular, the other is pneumonic or bronchopneumonic in type.

The gross distinction between these two types has, naturally, been made, with reasonable accuracy, by clinicians on the basis of physical examination and constitutional symptoms; but it cannot be denied that the clinician, during the last twenty years, has come to rely also, and to an extent which the more conservative man is sometimes loth to admit, upon the help of the *x*-ray picture. *X*-ray technic, in the hands of specialists, has now reached a high state of perfection. I need only refer to the beautiful work of Kennon Dunham in this country and of Graeff and Kuepferle in Germany. In regard to the present question of the distinction between the exudative and productive forms of lung tuberculosis, we are told that in most cases the *x*-ray picture is able to settle the matter. On account of the surrounding fluid exudate, the *x*-ray picture of the lesion in the exudative form shows a foggy outline, while the tendency to fibrosis of the productive form is represented by a sharp outline. Taken rigidly, so sharp a distinction is not always justifiable. At least, if one is to make it, the technical details must be absolutely identical in successive pictures. Varying degrees of lung inflation, the distance from the plate of any given tubercle, differences in development, constitute variable factors which may give confusing pictures. And at best the *x*-ray picture can only be accepted as one among several factors in coming to a decision concerning the type of lesion present.

A further consideration lies in this, that the two forms are frequently simultaneously present, with one of them predominating; or that they succeed each other. Although I lack that intimate knowledge of the clinical course of tuberculosis in its medical aspect which is enjoyed by the sanitarium expert, and is the legitimate fruit of long and close observation, I cannot but believe, with Sauerbruch, that the fundamental factor controlling the progress of the disease is afforded by the natural resistance of the individual patient, and that in general, whether in casting a prognosis or in considering the danger and the benefit of operation, we must be guided by the principle that the exudative form represents activity and a poor defense, and is consequently dangerous, while the productive form means chronicity, a good defense, and therefore relative safety. Resistance is the keynote to prognosis, and I would

like to say with all the emphasis at my command, that in respect of surgical operations upon the tuberculous patient, some evidence of resistance must be demanded. Upon that rock must the *ecclesia* of surgical treatment in this disease be built.

Now the evidence of resistance on the pathological side can be summarized in one word—scar. The end of all injury, the end of all disease which has produced destruction of any degree, is scar; and the scar comes through fibrosis. In this sense one may, in a measure and for practical purposes, disregard the various pathological and clinical classifications of the pulmonary tuberculous lesion. The use of such terms as "acinar-productive," "acinarnodose," "acinar-exudative," "lobar-caseating," "lobular-caseating," "cirrhotic," "fibroid," "ulcerative," and so on, while indispensable for anatomical descriptions, may be in large measure left aside by the internist or the surgeon, when the question of operation has to be decided, provided the evidence of a reasonable attempt on the part of the patient to control his disease, through fibrosis and scar contraction, is found. This is the least common denominator. Practically it means some healing, preferably a good deal of healing, and not too great destruction. How, then, are we to arrive, in practice, at a precise estimate of healing? The building has four cornerstones: clinical course, constitutional symptoms, physical examination and the *x*-ray picture. It is obvious that in respect of all these judgment, in the first instance, and indeed mainly, belongs to the province of the specialist in pulmonary tuberculosis, or of the trained internist; and the majority of patients hitherto referred to the surgeon for operation, have come from sanatoria. Is the surgeon, then, to play the rather minor rôle of carpenter? That is neither necessary nor advisable. As a matter of fact, while the original conception of a surgical operation for certain cases of pulmonary tuberculosis came from a medical man, the chief advance in our knowledge, not only of surgical technic but of indications, contraindications, prognosis and therapeutic results, has come from a surgeon. The surgeon draws from a whole circle of internists. Contrast, for instance, the experience of Sauerbruch, with his grand total of over 700 cases of thoracoplasty, with the necessarily limited experience of any one of his numerous "feeders." It is obvious that the judgment based upon such an experience must acquire a particular value. But the corollary is no less obvious; that the surgeon must himself become somewhat of an internist. He must

at least be familiar with the pathology and the general clinical course of the disease; otherwise he remains a carpenter. The age of individualization is past, and this generation is witnessing an extraordinary development of coöperation or teamwork in all branches of human endeavor. The internist and the surgeon must work together for the best results. What the surgeon expects from the internist is a knowledge of what surgery, as a branch of therapeutics, as a tool in his therapeutical armamentarium, can accomplish in selected cases. After this, that part of the internist's contribution to the combined effort is a precise estimate of the patient's resistance as shown by the history of the case and an informed opinion upon the probable course of the disease under eventual continuation of purely medical treatment. The surgeon's contribution is an estimate of the patient's resistance to the operation proposed and of the probable ultimate result of such an operation.

We may now proceed to discuss very briefly the indications for operation. It is to be understood, first of all, that we are concerned only with pulmonary phthisis as seen in late adolescence and the adult. In one word the most favorable type is that of the "good chronic." The incipient and the very advanced cases are obviously out of the question. In one the evidence of resistance has yet to be proved. In the other it has failed. Likewise one must exclude the acute exudative, bronchopneumonic or lobar-pneumonic phthisis, for in these resistance is either overcome or is most uncertain. The chronics, then, who have given proof of defensive powers by the very fact that they are chronics, constitute the greater part of the surgical field. Even the bad chronic, with considerable cavitation, fever, rapid pulse, and showing general symptoms of "slipping," may be accepted, provided he afford the evidence of scar contraction in reasonable degree. What we look for is the contracted chest. That this contraction should be unilateral, that the other lung should be sufficiently sound to carry on the work of respiration after operation has abolished whatever respiratory function the sick lung is still performing, is a self-evident proposition. What then are the signs of a unilaterally contracted chest? They are sufficiently familiar to all: A falling-in of the rib spaces and of the clavicular fossæ, a pulling up of the diaphragm, a pulling across toward the affected side of trachea, mediastinum and heart, and a narrowing of the intercostal spaces. The pleural space is

frequently obliterated by adhesions. Bands of scar tissue traverse the lung and are attached at one side of an unyielding bony thorax, and on other sides of the periphery, to a thickened pleura and mediastinum. By these cavities are held open. There is everywhere

Fig. 1.—Case I, H. P. Before lipiodol injection. Chronic case with fibrosis and cavitation on left. Note two cavities under clavicle and under lower end of scapula. Lower lobe changes obscured by diffuse shadow. Right lung good.

the evidence of tension. Scar has contracted to its limit. There is no help to be seen save in the further yielding of some structure. The opposite healthy lung has yielded as far as possible and become emphysematous. The sick lung, the trachea, mediastinum, heart and diaphragm have come across as far as they can. Even the ribs

have given as far as possible. But the chief blame still falls on them. They are the innocent guilty. If they cannot yield further, their good will must not be counted to them as a saving grace. It is

FIG. 2.—Case I, H. P. After lipiodol injection. Note extensive bronchiectasis in lower lobe. The lower cavity is partly filled with the lipiodol, but this has not reached the upper one. The value of the method in this case lies chiefly in revealing the lower lobe bronchiectasis; also in demonstrating the lower cavity as cavity and not a possible localized pneumothorax.

obvious that they must be cut off and their generation know them no more. Metaphor aside, such is the *raison d'être* of the operation. That being done, relief of tension is afforded. It is an "entspannung" in a very real sense. To this release there is added an actual

compression of the lung substance through the falling on of the rib stumps, and, what is of still greater importance, the lung is put at rest. The walls of cavities are brought together, or at any rate closer together; minute cavities are obliterated; the blood

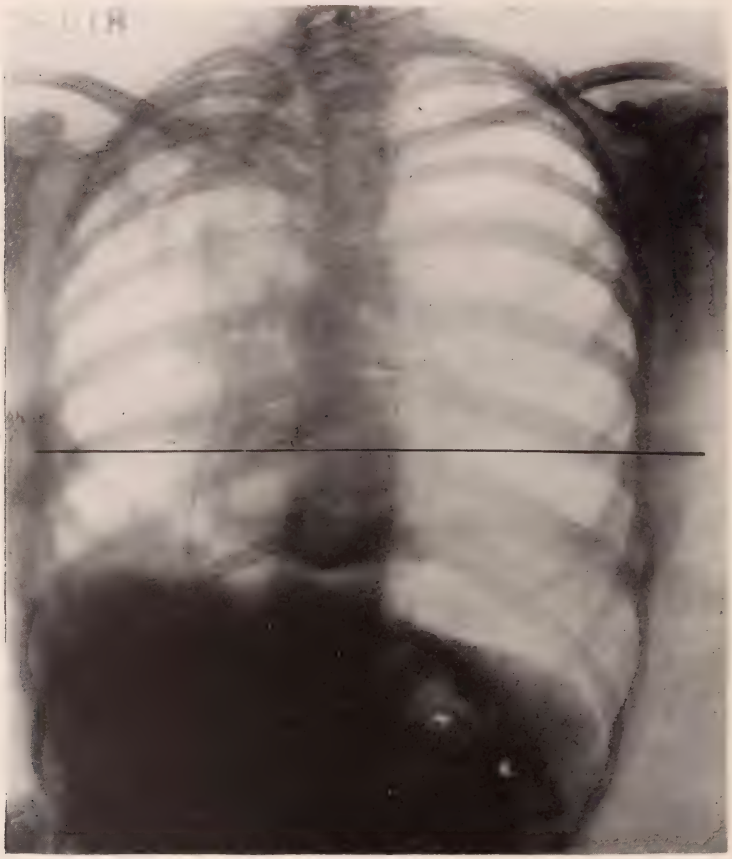

FIG. 3.—Case II, Miss L. Before lipiodol injection. Pulmonary tuberculosis with considerable cavitation and fibrosis, in right upper lobe chiefly. Cavity is not well seen in the original film. Left side quite good.

circulation is altered, though in which direction we are not quite sure; the lymph circulation is certainly slowed; the air circulation is reduced; the absorption of toxins is retarded or prevented; the fibrosis of hyperemia and of air emptiness is encouraged, and, in

short, nature takes a fresh grip and is given a chance to proceed with her ordinary work of scar formation.

We may turn now to a short consideration of the pathological changes that develop in the compressed lung after the operation of

FIG. 4.—Case II, Miss L. After lipiodol injection. Note deflection of trachea, marked bronchiectasis near the hilus, and a cavity below the clavicle fairly well filled. Injection on left side shows normal hilus.

thoracoplasty or after the institution of a complete pneumothorax. One's hope, of course, is that the sclerosing process of low-grade inflammation, which was in evidence before operation, will continue; and, as a matter of fact, the end-result in the favorable case is a small, solid, fibroid lung, like a spleen. But it is interesting to inquire by what

particular new agencies this result is brought about, and in what way extension of the disease is prevented. Fibrosis in the lung before operation is certainly due to chronic, low-grade inflammation, the

Fig. 5.—Case III, Mr. R.: Before injection of lipiodol. The patient had a partial thoracoplasty done, in another city, two years previously, with removal of fourth to ninth ribs inclusive. Symptoms were only partly relieved. Note the impossibility of discovery, with the ordinary film, the exact lesion present, on account of the partial lung compression. The right lung shows a few old lesions.

response on the part of the tissue of the host to the attack of the bacilli. We cannot assume that that attack is immediately stopped by the new condition of lung collapse following operation. And

a part of the fibrosis succeeding operation must be ascribed to this factor. But experiment has shown that fibrous tissue is laid down even in the normal lung under certain conditions in which inflamma-

FIG. 6.—Case III, Mr. R. After lipiodol injection. There is seen in the upper lobe a cavity partly filled with the oil, and beneath this dilated bronchi or narrow irregular cavity. In the lower lobe, from the hilus down, there is a mass of dilated bronchi. The injection on the right side shows normal hilus and lung.

tion has nothing to say. And these conditions are, briefly: Air emptiness, venous stagnation and lymph stagnation. Taking this last first, one need only refer to the general thickening of subcu-

taneous tissue so commonly seen after prolonged use of Bier's hyperemia, or as in elephantiasis. That stagnation of lymph takes place in the compressed lung is now generally agreed. Tendeloo and Naegeli both showed that the lymph circulation is largely depen-

FIG. 7.—Case IV, K. W. Before lipiodol injection. Total thoracoplasty done, on right side, three years ago with great improvement. Recurrence of cough and sputum with chronic fever during last few months. Note impossibility of making out in the ordinary film any particular lesion.

dent upon lung movement and that if this were stopped the lymph-flow was much retarded. Shingu demonstrated that soot, which by way of aspiration had entered the lung tissue, was more slowly worked out of the lung in the compressed than in the uncompressed

lung, and this was confirmed by Naegeli, and by Bruns and Kistler; and more recently Gardner has found also a great widening of the lymphatics in microscopic sections. To this feature we ascribe a large share of the lessening of toxemia observed after lung compres-

FIG. 8.—Case IV, K. W. After lipiodol injection. Note the cavity in the upper lobe, just below clavicle, and below this bronchiectasis in the lower lobe extending down from the hilus. The left lung is practically normal. In no other way than by lipiodol injection could such residual lesions be demonstrated.

sion. In experimental work the condition of air emptiness, or atelectasis, has been obtained by permanent ligature of the main bronchus to a lobe. Within twenty-four hours, if the chest be reopened, it is found that the lobe concerned is quite collapsed and apparently

solid.[1] In the course of time a large amount of fibrous tissue is deposited throughout the lobe. The same process has been observed to occur in the human under conditions which cause an obstruction of the main bronchus of a lobe.

The effect of compression of a lung upon the bloodflow through it has been the subject of much inquiry, partly experimental, partly clinical. Bruns and Sauerbruch, years ago, found that ligation of the pulmonary artery results in a marked laying down of fibrous tissue, and Tiegel demonstrated that this was also true of the condition of venous stagnation which he brought about in animals by placing constricting bands around the pulmonary veins. This work has recently been confirmed by Schlaepfer. Upon the basis of this experimental work, Kornfeld, quoted by Schlaepfer, appears to have ligated the pulmonary artery in a case of pulmonary tuberculosis, with large abscess of the lower lobe, and claimed a cure. Whether the lung compressed by a good pneumothorax or a good thoracoplasty receives a greater or a lesser blood circulation appears to be still unsettled. Sauerbruch concluded that the circulation was increased and in this was supported by Cloetta's experiments. Bruns, Lohmann and Müller maintained the contrary, that the circulation was diminished, but the experiments of Cloetta and Ruge seem to be the more convincing, and we may assume that in the condition of lung collapse there is a definitely increased amount of blood in the alveolar septa. This, however, points rather to stagnation, and Bruns's conclusion is that practically the lung which is under long-continued compression by a pneumothorax, in consequence of the permanent atelectasis and the greater increase of fibrosis, receives a subnormal blood circulation.

It is fairly certain that for practical purposes, and particularly in the condition of lung compression as the result of thoracoplasty, all these causes are operative in varying degree. Yet, we are not certain that the compressed lung is really completely empty of air as regards its alveolar area, and we must believe that the larger bronchi and bronchioles remain, to some extent, patent.

Recent work by Giraud and de Reynier, who injected lipiodol into tuberculous lungs long compressed by a total pneumothorax, showed that the lipiodol penetrated more or less freely the bronchial tree and filled even the alveoli to a considerable extent. He argues

[1] F. A. C. Scrimger: Unpublished experimental work upon massive collapse. Personal communication.

therefore that, in explaining the good effect of pneumothorax, the older arguments based on cessation of air circulation, compression of alveoli, prevention of dust aspiration and of a bronchial spread of infection are invalidated, and he falls back upon the theory of changes induced in the vascular and lymphatic circulation. Our observations with lipiodol in old cases of thoracoplasty do not tend to confirm this statement. The alveolar district was not filled, but only cavities and dilated bronchi. But Corper and his co-workers have also shown experimentally that bacilli injected intravenously in rabbits, under the condition of a one-sided total pneumothorax of one month's duration, are deposited about equally in the compressed and the uncompressed lung, and these progress to massive tuberculosis equally on both sides. The arterial circulation, therefore, is not impeded by compression. This contradicts the earlier work of Tiegel, who claimed that in the artificially compressed lung the extension of an experimental tuberculosis did not succeed.

In the presence of these contradictory statements we have to fall back upon the practical observations of pathologically examined lungs that have been subject to compression either from pneumothorax or from thoracoplasty, and such observations have been uniformly to the effect that the chronic compressed lung is hard, firm and atelectatic. We feel sure that no great respiratory exchange goes on in the alveoli of such lungs, even though, perhaps they may be partly filled under the pressure of cough by lipiodol introduced into a main bronchus. We may also feel certain that as in all fibrosed organs the blood circulation is relatively hindered by the very fact of fibrosis, which is apt to obstruct many of the capillaries. And finally the stasis of lymph has been definitely demonstrated in pathological sections. Exactly what part these three factors may play in the ultimate good results of new fibrosis it is difficult to say. All these things probably work together. The main fact remains that operation does in many instances bring about an arrest of the disease through fibrosis.

Returning then to our original conception of the pathology of the lung as concerned with the selection of cases for operation, I would put it in this way: If, as the result of consultation with the competent internist and a careful consideration of the clinical course, physical findings and *x*-ray films (if possible, a complete series of these), it is determined that the chiefly affected lung (very rarely is

the disease strictly unilateral) is tending strongly to healing through fibrotic contraction, but is prevented from complete healing by cavitation or by insufficient yielding of surrounding structures, then the operation of thoracoplasty is indicated. Pneumothorax has usually been tried and found impossible or insufficient.[1] Here we have the uncomplicated picture of the chronic productive form. There are, nevertheless certain cases of this form that are unsuitable; they are those that show excessive cavitation. Numerous small cavities of the honeycomb type may be accepted; the single large cavity at the apex also. These frequently heal after a thoracoplasty. But several large cavities in both lobes constitute, in my experience, too big a task. Such patients can be brought safely through the operation, but the ultimate result at best is a degree of improvement which hardly compensates for the suffering endured. These patients are the rather desperate and despairing old chronics of many years' sanitarium residence, who are recognized as only hanging on to life by their teeth. A second class consists of the "chronics" who for several weeks or months have shown signs of activity. These are the mixed forms of productive and exudative lesion. One is sometimes in doubt whether the fever, pulse, sweats, etc., are caused by active exudative tuberculosis or by a mixed infection. Here one is helped by the $x$-ray picture and by the experience of the tuberculosis specialist. Operation is allowable for either. But if decision leans to the side of tuberculous activity, extra caution is needed to exclude the beginning of active tuberculosis in the good lung. If any such suspicion exists, particularly if any lesion can be demonstrated in the opposite hilus or lower lobe, thoracoplasty should be avoided and every effort made to establish a pneumothorax, or a phrenicotomy alone should be done, because the strain of thoracoplasty is so very apt to be followed by rapid exacerbation of the disease in the good lung. Here a pneumothorax, while unsuitable as a permanent form of treatment, is valuable in allaying activity and tiding the patient over into a renewed chronicity with productive tendency, and to a later thoracoplasty. On the continent such cases have been frequently subjected to operation, and sometimes to operation in one stage. Sauerbruch and Brunner recognize

[1] I reserve pneumothorax for active, exudative disease, either original or complicating a chronic productive process, believing it to be for the pure chronic case both insufficient, ultimately, and not without danger.

freely that they constitute poor operative risks whenever the exudative form holds the upper hand and that good results are most infrequent. I also have operated on a number of patients of this type. But I am sure it is wiser to avoid them or at least postpone them. Operation is a greater strain than phrenicotomy or artificial pneumothorax. Use these for a while; or even trust to Nature, with the help of a bed-rest which must be as absolute as for Pott's disease; and the patient is given, I believe, a better chance than with operation. If he does not improve, he would not do so with operation, and operation may tumble him on the wrong side of the fence.

If all this is true, how much more is it true of the class of acute exudative, progressive tuberculosis coming on fairly early in the disease, even if apparently confined to one side! These show no evidence of fibrosis and scar. I do not operate if trachea and heart are in their normal position. It is fortunate that in this class pleural adhesions are usually absent, and the good effect (often indeed miraculous effect) of lung compression and rest can be more safely secured by artificial pneumothorax. And yet many even of these have been operated on "to give them their chance." The results have been desolating—a high operative mortality, a low percentage of "improvement," and of "practical cures," *nil*. To this attitude I have been led by certain sad experiences, fortunately few. Here, then, lies the main point of this lecture: If this operation is to be practised widely in this country I trust that its good name will not be blackened by an excessive mortality due to ignorance of the character of the pathological lesion present in these less favorable types. It is not sufficient that the disease should be apparently unilateral or nearly so. The evidence of resistance in scar contraction must be first demanded. *Do not operate if the trachea is in the midline.*

The Results of Surgical Treatment. In considering the question of results I shall confine myself to a presentation of personal experience set down in tabular form. One must deprecate the drawing of too rigid conclusions in respect of improvements and practical cures; the personal equation varies too much. But as to mortality, here at least figures are not deceiving. And I feel justified in calling attention to the low mortality-rate ascribable to the operative act, calculated for a limit of two months, as adopted arbitrarily by most authors. The operation can no longer be

considered a formidable or very hazardous one, provided the cases are selected on the proper basis.

And as to the late mortality, it may be said with confidence that in nearly all cases death has not been hastened by the operation, but is rather due to the progress of the disease, which operation has failed to halt or halted only temporarily.

Lipiodol Injection of the Tuberculous Lung. I pass to a very brief consideration of lipiodol injections in tuberculous lungs. For a general consideration of the subject I must refer you to recent articles published by Dr. David Ballon and myself in the *Canadian Medical Association Journal* for 1925. I would like here to express my great obligation to Dr. Ballon for his very great help, and indirectly also to Dr. Chevalier Jackson, from whom Dr. Ballon, like so many others, received instruction and inspiration. Dr. Clerf, of the Jackson clinic, has also recently published an excellent article on this subject of pneumography. I do not feel yet prepared to recommend the use of lipiodol injections in all, or even in many, patients with tuberculosis who present themselves for operation. Sergent and others, of the French school, advise indeed against its use, fearing a stirring-up of disease by the liberated iodine. In my series of 10 tuberculous cases we have noted two "reactions," with fever and rapid pulse, lasting from a few days to a week, followed by return to normal. This has not appeared to do any lasting harm. Nor have symptoms of iodism been observed. But in a total of about 45 cases injected by Dr. Ballon there occurred 1 sudden death during bronchoscopy after instillation of about 15 cc. of lipiodol. Postmortem failed to determine the cause of death. The patient was recovering from what was supposed to be an indefinite pneumonia on both sides, and cavitation was suspected. The autopsy showed a tuberculous bronchopneumonia on one side and a nontuberculous bronchopneumonia on the other. It was set down provisionally as a cocaine poisoning, or possibly a sort of pleural shock. *X*-ray of the head did not reveal lipiodol in the cerebral vessels. On the other hand, there are great advantages to be got from the method, particularly in the diagnosis of the unclear forms of lung infection. It is astounding at times to see revealed extensive bronchiectasis, especially behind the heart and below the dome of the diaphragm, which from physical signs and the ordinary *x*-ray film one could do no more than suspect. The

same is true of abscesses and of mixed bronchiectasis and abscess. In respect of tuberculosis, the demonstration of residual lesions after thoracoplasty both as to character and localization is hardly possible by any other method. It allows one to determine whether further operation is justifiable or not. If a further operation is attempted (and of this we have as yet very little experience) the method will allow of some reasonable control of the results obtained. In addition it is possible, in cases that come up for an opinion as to the advisability of thoracoplasty, when the ordinary *x*-ray pictures give us no detailed information about the condition of the lung owing to dense shadows, to demonstrate with lipiodol the presence or absence of cavitation and bronchiectasis. One looks forward also to its use in differentiating between localized pneumothorax and intrapulmonary cavity, a distinction which is frequently difficult to make. The demonstration of a bronchial fistula communicating with a tuberculous pneumothorax may also be made by this method and possibly the exact site of the fistulous opening. This, at least, was obtained in a case of nontuberculous chronic empyema. The problem of annular shadows may, in some measure, be resolved by this method. These are a few of the possibilities; others will doubtless appear with increasing experience.

We have up to the present made use of lipiodol in 10 cases of pulmonary tuberculosis, in 3 of which the lung had previously been compressed by a thoracoplasty. With regard to these last, I have examined the films particularly with reference to the question whether the lipiodol would fill or would not fill the compressed lung tissue. No definite conclusion could be formulated. In each case the amount injected filled only residual cavities or dilated bronchi and did not penetrate the rest of the lung. It is possible that an insufficient amount was used, but even in small amounts we are accustomed to see the stuff forced out of cavities by posturing or by cough and appear in the smaller bronchi and the alveoli over considerable tracts of healthy lung. In the compressed lung no sign of this was seen, and I am inclined to think that the compression resulting from thoracoplasty had obliterated the finer air passages of the lung. In the remainder of this small series the lipiodol was injected with the purpose of attempting to show the extent of cavity formation or of bronchiectasis, not only in order to form a more accurate estimate of the destruction that had occurred, but

also for comparison with pictures that might be taken after the lapse of years in order to determine more accurately the indications for operation in lungs that show considerable destruction. It was hoped, also, that a more exact estimate could be made of the anatomical site of cavities in stereo pictures, particularly with regard to the situation of these in the neighborhood of the hilus, where, as we are accustomed to think, compression therapy exercises its least effect. Up to the present I do not feel competent to say anything of a definite nature. The work is still too young, but I trust that the pictures which I now proceed to show will be sufficiently new to arouse your interest and sufficiently clear to demonstrate the possibilities of the method.

SUMMARY OF 83 CASES TREATED, DIVIDED AS FOLLOWS:

| | |
|---|---|
| Extrapleural thoracoplasty, posterior: | |
| (*a*) Total (resection of ribs from top to bottom) | 50 |
| (*b*) Partial (resection of half the ribs, maintaining usually a pneumothorax over other half of lung) | 9 |
| (*c*) Posterior thoracoplasty, with addition of apicolysis in front, in three stages | 6 |
| (*d*) Anterior thoracoplasty, total (following posterior thoracoplasty three years before), with phrenicotomy | 1 |
| Phrenicotomy (as the only operation) | 4 |
| Cutting intrapleural adhesion to improve an existing pneumothorax | 4 |
| Pyopneumothorax | 9 |

DEATHS WITHIN TWO MONTHS ASCRIBABLE TO THORACOPLASTIC OPERATIONS (EXCLUSIVE OF PYOPNEUMOTHORAX CASES.)

| No. of cases. | | No. of operations. | Time. | Cases. | Deaths, per cent of cases. | Per cent of operations. | Cause of death. |
|---|---|---|---|---|---|---|---|
| Total posterior, | 56 | 122 | 1st week | 0 | 0 | 0 | |
| | | | 2d " | 2 | 3.0 | 1.64 | Ac. lobar pneumo. Cardiac failure. |
| | | | 3d " | 1 | 1.5 | .82 | Strep. abscess. |
| Partial posterior, | 9 | | 7th " | 1 | 1.5 | 0.82 | Tb. pneumonia. |
| Total | 65 | ... | ... | 4 | 6.0 | 3.28 | |

In 6 of these 65 an apicolysis was done at intervals of six weeks to two and one-half years after the posterior thoracoplasty. Of these 3 patients died within two weeks. All 3 had very advanced cavitation with fibrosis throughout the lung and were in desperate condition. The operation of apicolysis in such cases should be avoided. These deaths are not included in this table, which includes only the standard operation. They properly come under "deaths from progress of disease."

## LATE DEATHS NOT ASCRIBABLE TO OPERATION OF POSTERIOR THORACOPLASTY.

| | |
|---|---|
| In second month (from typhoid contracted in hospital after good recovery from two-stage thoracoplasty) | 1 |
| During first year (from progress of disease) | 3 |
| During second year (from progress of disease) | 4 |
| During third year (from progress of disease) | 1 |
| During fifth year (from progress of disease) | 1 |
| Total | 10 |
| During first two weeks after apicolysis, a third operation following the two-stage posterior thoracoplasty | 3 |
| Total number of deaths | 13 |

Total number of cases, 65 (20 per cent).

## GENERAL RESULTS FOLLOWING THE OPERATION OF THORACOPLASTY, TOTAL, PARTIAL, OR WITH ADDITION OF APICOLYSIS.

| *Over One Year*, 44 *Cases* | | *Under One Year*, 21 *Cases* | |
|---|---|---|---|
| Practical cures | 15 (34 per cent) | Greatly improved | 6 (29 per cent) |
| Greatly improved | 8 (18 " ) | Improved (4 still in hospital) | 12 (58 " ) |
| Improved | 4 ( 9 " ) | Stationary or worse | 0 |
| Worse | 1 ( 2 " ) | | |

| *Deaths* | | *Deaths* | |
|---|---|---|---|
| First three weeks | 2 ( 5 per cent) | First three weeks | 1 |
| Second month on | 14 (32 " ) | Late | 2 |

| | |
|---|---|
| Encouraging results (cures and improved) | 45 in 65 cases (70 per cent) |
| Discouraging results (worse or died) | 20 in 65 cases (30 per cent) |

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# THE ADVANCEMENT OF EPIDEMIOLOGY THROUGH EXPERIMENT*

## The S. Weir Mitchell Oration

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NEW YORK CITY

(From the Rockefeller Institute for Medical Research, New York)

## I.

You have conferred a great honor upon me in inviting me to deliver the oration established in memory of the remarkable services of Doctor Weir Mitchell to science and to the public welfare. I know of no more fitting way to perpetuate the name and deeds of a man of science than by the creation of such an endowment as this. I wish that I felt better fitted to discharge the onerous duties of the occasion. But as one who was privileged to know Doctor Mitchell intimately and to come directly under the influence of his inspiration, I am very happy to be so circumstanced as to pay him tribute. Doctor Mitchell's deeds have added and will long continue to add luster to the city of Philadelphia; to the medical profession which he adorned; to the science of physiology from which, it is true, he withdrew for the wider field of neurology, but which nevertheless he never deserted nor ceased to love, and which either directly or indirectly he continued to enrich throughout his long, varied, and brilliant career; and finally to literature, to which he devoted those lighter hours of repose that the regularly recurring summer season brought into his busy life. Knowing Doctor Mitchell as I did, and his intense preoccupation with the nature of disease, I am constrained to believe that he would have been deeply interested in the theme of this evening's lecture. Since he never failed to follow the current of scientific progress, he would, I am confident, have wel-

* Read December 16, 1925.

comed the effort now being made to bring light and order into the vexed subject of epidemiology by seeking for it an experimental basis.

Within the quarter century just closing, the United States together with many other countries has been passing through four considerable epidemics of disease—of cerebrospinal meningitis, poliomyelitis, influenza, and epidemic encephalitis. Each of these plagues has, either in turn or contemporaneously, claimed many victims, and excepting perhaps epidemic influenza, none of them has definitely run its course. The ravages still continue, and it is indeed not to be predicted when they are to cease and the conditions prevailing before their appearance be resumed.

There is small wonder, therefore, that the study of epidemiology should have come again to the front. A sorely harassed world is awaiting anxiously, as it were, a satisfactory answer to the question of the nature and the source of these pestilences of mankind. The question is of course not a new one and already not a few answers, none really adequate, have been made to it. But the state of the medical sciences at the present day would seem to give hope that knowledge not hitherto available may be secured from a fresh attempt at the solution of the biological problems involved.

We turn back to the father of medicine, as Hippocrates is admiringly and affectionately called, for the first recorded observations on the epidemic occurrences of disease. For it is true that the chapters on epidemics in his works consist of observations in which clinical course and states of the weather are considered in mutual relationship. Through this, then novel, way of viewing the onset and the symptoms of disease arose the doctrine of epidemic constitution, which has since played a major, if fitful part, in the history of epidemics. In developing this concept as applied either to climatic conditions of such marked type as to give a distinguishing character to a period of time, or to denote a fixed type of disease prevalent at a particular time, Hippocrates described actual occurrences which later writers translated into theories of the epidemic.[1]

The further development of the concept of epidemic constitution as a controlling or determining agency in bringing about the rise and fall of disease is attributed to Ballonius and to Sydenham.[2] The writings of the latter are more familiar to us and Sydenham's name is intimately associated in our minds with the doctrine. According to him, the potent influences are engendered through

occult and inexplicable changes in the atmosphere and are of a mysterious, so-called "skiey" nature, which determine the duration and devastation of the prevailing disease. The constitutions differ in different years, depending upon hidden changes in the bowels of the earth, through which the atmosphere becomes contaminated and the bodies of men predisposed and made subject to this or that disease. A particular disease continues during the influence of a certain constitution, which after a cycle of a few years gives ground and makes way for another.[3]

All this may sound to us extremely mythical, and yet very recently the concept of constitution has been, indeed is being, reasserted in very respectable epidemiological quarters, in order to explain the epidemic happenings of the past twenty-five years. The question has been put whether in this period just such a cyclic succession of diseases and of constitutions, having a world-wide distribution, has not been taking place. Now it may be said, without any comment in advance, that it is not improbable that a doctrine so vital as that of epidemic constitution has shown itself to be, may after all, and in spite of certain vaguenesses and repellant features, still contain a morsel of precious truth, the detection and elucidation of which may be essential to a complete understanding of the nature of the processes—biological and physical—on which the occurrence of epidemics depends.

In Sydenham's day, the science of statistics was in its infancy in England and had not yet been born elsewhere.[4] With its rise and with the study of the written records of epidemics, there arose a new outlook in epidemiology which may be called the statistical-geographical, and which culminated, as it were, in the publication of Hirsch's great work between 1860 and 1864 on historical geographical pathology.[5] As presaging coming events which ushered in the bacteriological era, there appeared within this period two remarkable papers dealing with the innate nature of infectious disease, and postulating with a certainty and completeness not before attained the necessary or causal relation of microörganisms to the processes. I refer to Henle's epochal paper, "On miasms and contagia" of 1840 and the less celebrated one by Griesinger on "Typhus, typhoid, relapsing and malarial fevers," published between 1857 and 1864.[6]

Hard on the heels of Hirsch's monumental work came the epochal discoveries of Pasteur and Koch, their pupils and successors, which

quickly transformed the entire scientific and practical outlook on the infectious diseases. The extraordinary discoveries in bacteriology, which now followed in almost bewildering rapidity of succession, raised strong hopes that the inner nature of the epidemic would be quickly revealed, a premature expectation which I need not tell this audience has not been entirely realized.

And yet the gains even within this field have not been small. I need merely to allude to the detection of the insect vectors of disease and the diminution brought about through the practical application of this knowledge to malaria, which in many places has been thus and for the first time brought under control, and to yellow fever which has in the same manner been almost eradicated. Furthermore, through an adequately, scientifically based system of water purification, typhoid fever has been made to vanish from many strongholds, and the menace to the West of cholera has been reduced to impotence. The discovery of the power of protective inoculation has served still further to diminish the incidence of typhoid fever and allied diseases, and of diphtheria; and the detection of the healthy and other carriers of disease-producing germs has been rewarded by still further material reductions.

And yet we are so far from a complete understanding of the nature of infection in all its variegated and intricate forms as to be in certain instances, in epidemic influenza for example, impotent to affect its essentially undeviating course. The masters of bacteriology early perceived that infection is a process more subtle than the resultant of a mere bringing together of, on the one hand pathogenic microbe, and on the other susceptible host; and that about those factors played a series of adjusted biological reactions which ever since and increasingly it has become the task of the bacteriologist to disentangle. Somewhere within this field, once it is wholly won over to knowledge, lie the opportunity and the power to interfere with precision and certainty for the control of epidemic disease.

The discrepancy between the power of the microbe to strike and that of the host to defend led to the formulation of certain counter theories of the epidemic, in opposition to the purely bacteriological or etiological one coming into vogue. The counter theories still play a part in the history of epidemiology and, in one form or another, continue to be invoked, as has indeed just been done by Wolter in the case of the soil theory of von Pettenkofer, to account

(I believe erroneously), in Russia especially, for postwar epidemics of typhus and other diseases which are, I think, more satisfactorily explained on the basis of famine, louse infestation, and like causes.[7] This notion put forward by von Pettenkofer postulates a certain prepared state, contamination or what not, of the soil as a forerunner and concomitant of epidemics, especially (although not exclusively) epidemics of typhoid fever and cholera. The theory has, with growing knowledge and improved communal sanitation, steadily lost ground and its revival seems inopportune and is not likely to bar real progress. On the other hand, Nägeli's diplastic theory, so-called, which assumes the coördination of two microbes—one, as we should now say, the specific, etiological incitant, visible, cultivatable, and so forth; and another, hypothetical and probably ultramicroscopic—has received an unexpected ally recently in Hamer, the British epidemiologist, who sees in the class of filter-passing organisms the second essential factor in the partnership. Basing this view on de Schweinitz's discovery of the virus of hog cholera, Hamer constructs an imaginary pathology of influenza and other epidemic diseases, in which the filter-passer determines the kind of action which the specific, more obvious incitant, as for example the Pfeiffer bacillus, shall perform.[8]

We may discern in these revivals—epidemic constitution, contamination of the soil, coöperative or symbiotic action—the serious difficulties under which present-day epidemiologists are contending in the effort to bring light and order into the discussion of the nature and origin of the epidemic. The statistician too is groping more or less in the dark. The science of statistics has grown amazingly since Sydenham's day, and it is applied to an ever-widening circle of happenings, and often doubtless with remarkable results. As applied to epidemiology, we are enabled to envisage the perturbation of epidemic disease as never before: We follow now its imminence, onset, rise, and decline on a world-wide scale. By substituting, to use Greenwood's phrase, the herd for the individual, through depersonalization of disease phenomena, we have undoubtedly procured a body of data for analysis leading sometimes to useful or suggestive deduction. To mention one or two examples only, one thinks of Farr's generalization of the course of the epidemic in cattle plague in England, and Brownlee's hypothesis of a life cycle of the measles or other incitant, still awaiting discovery, which controls the appearance, disappearance, and reappearance of epidemic outbreaks of measles and possibly of other diseases.[9]

The bacteriological era in epidemiology is distinguished from its predecessors particularly by reason of the concept of strict specificity, or the operation of a particular microörganismal agent in producing a definite disease. In this important respect, the periods before and after Pasteur and Koch are widely separated. The isolation of tubercle, typhoid, and diphtheria bacilli, of trypanosomes and spirochetes, and a whole host of other microbes intimately associated with cases of infectious disease, and their clear biological distinction one from the other, led to the conviction of a particular parasite as the incitant of a particular disease. The strength of this belief in specificity is reflected in Koch's dictum that the parasite must always be found at the seat of disease and in the sick, but not in the healthy individual. In view of the frequency with which so-called "carriers" of pathogenic microbes are to be detected even among the healthy, this exclusive doctrine is no longer tenable, although it may not be affirmed that the newer discoveries in this field have severely shaken the concept of specificity. Rather it may be asserted that they have widened the outlook and led not only to the solution of riddles, otherwise unsolvable, in local outbreaks of infectious disease, but they have served to emphasize strongly the coördinate nature of infection and the interplay of forces as between microbe and host of previously unsuspected intricacy.

Up to this time the second partner, or host, had accorded him a subordinate, if not a relatively insignificant rôle. It became apparent, however, that not all individuals or groups equally exposed, equally responded to the exposure, and that with many epidemic diseases, sometimes racial, sometimes other characteristics seem to play determining parts. In regions in South America where yellow fever raged periodically, the dark or native population was observed to suffer less than the white immigrants, and the newly arrived among the latter oftener became victims than those already established or acclimated. Among animals, too, as in the notable instance of insusceptibility of Algerian sheep to anthrax infection, such distinctions have existed. Whatever, therefore, might be thought regarding the activity of the microbic agents of disease, it was obvious that the host material is not an homogeneous one, and that previous and prolonged exposure to an epidemic disease does tend to decrease danger of attack.

The detection of carriers and especially the greater refinements of the bacteriological technic in revealing microbes potentially pathogenic as forming groups rather than as composed of sharply cut species, raised the questions whether they also do not show more or less heterogeneity. A vast literature on this subject has already come into existence and to it there are made almost daily additions, the sum of which has tended greatly to modify the older views of the fixity of bacterial strains. I desire to place emphasis on the point that in the brief description which follows, we are dealing not with the transformation of species, but rather with variation within given species, in which the ground or original type, phylogenetically speaking, remains undisturbed.

In 1902, de Vries announced mutation among the higher plants, and in 1906 M. Neisser and Massini described a mutating Bacillus coli which they termed "mutabilis." The twenty years intervening have witnesses the demarcation of large groups of related organisms, such as compose the dysentery and paratyphoid bacilli, and the pneumococci, streptococci, and meningococci—to mention only outstanding examples—in which distinctions are based on cultural, pathogenic, and immunological differences. Instability of type among certain bacterial groups and transition between types have often been asserted, but the conclusive evidences for such conversions have been slow in being brought forward. On the other hand, it is logical to suppose that with wide fluctuation among microbes, affecting even the quality of virulence, the possibility is to be reckoned with of particular variants (mutants?) of enhanced powers of infectivity, becoming dispersed and thus leading to epidemic outbreaks of disease.

The investigation of ordered variation or mutation among the bacteria was greatly advanced by de Kruif's observation of changes occurring in pure-line strains of the bacillus of rabbit septicemia (Bacterium lepisepticum) and of Arkwright's observations on Bacilli typhosus, paratyphosus, enteritidis, and dysenteriæ in 1921, through which the highly virulent S forms (growing in smooth colonies) become transformed into slightly virulent *R* forms (growing in rough colonies).* The two variants show immunological reactions more or less in common, but differ markedly in acid and

* De Kruif used the letters *D* (diffusely growing in broth) and *G* (granular growing) to designate the two forms. But Arkwright's designations *S* and *R* have now been generally adopted.

saline agglutination points. The *S* strains tend in different degrees to give off *R* strains, while the latter doubtfully revert to *S*. In the case of the bacillus of rabbit septicemia, more closely studied perhaps than any other bacterium in this respect, the change from *R* to *S* has not been detected. The $S \rightarrow R$ mutation of this bacillus has been shown by Webster to depend on the oxygen tension of the culture, and to be favored by free oxygen and inhibited by oxygen absorbing substances (hemoglobin, etc.) in the medium. Reimer and Amoss, independently of each other, have recently promoted by special procedures the passage of pure-line strains of pneumococcus type I *S* into type I *R*, but have not been successful in bringing about the reverse transformation.[10]

Nor is this all. The pneumococcus and streptococcus groups of bacteria are doubtless closely related, and the distinction between them has long been regarded as indefinite. If, therefore, we are to accept recent perhaps inconclusive reports of Neufeld and of Morgenroth, we must admit transformations within groups tending still further to obscure the dividing lines. Moreover, Jordan has even reported an instance of reversion of a pure-line paratyphoid *R* into *S*. Not impossibly not one variant only, but a series of $S \rightarrow R$ variants is given off by certain bacteria, some slightly, some fundamentally altered in relation to the parent strain, according to which degree the $R \rightarrow S$ reversion may or may not be accomplished. The studies in this fascinating field are progressing rapidly, and it will be well to withhold judgment and prediction until we are possessed of far fuller data than are at present available. I commend to those intending to embark on these somewhat troubled and tedious investigations, the utilization of pure-line strains only derived from single bacteria as procured by the Barber or an equivalent technic, and the employment of as precise and rigid bacteriological and immunological methods as may be possible.[11]

To the epidemiologist this new knowledge and direction of research come with special force and significance. As his purpose is to account for the origin as well as for the movements of the epidemic, the life history of the microbes concerned becomes of high importance. Mutation or variation being now established as a not uncommon phenomenon, the question arises whether the change goes only in the direction of more to less, or may also proceed in the direction of less to greater virulence. *The fact should, therefore, not be lost sight of that up to now the changes observed have been of the nature of*

*a degradation and not of an exaltation of pathogenicity*, and while it cannot of course be denied that the reverse process is capable of taking place, we must admit the lack of convincing evidence of its significant occurrence.

At this point I shall digress in order to present to you an instance of rise in power of the virus of poliomyelitis which came to the attention of Dr. Harold L. Amoss and myself. Unfortunately, the conditions under which the rise, fall, and second rise in the activity of the virus took place were not such as to permit any clear insight into the precise factors involved, as for example, whether merely one alone or several virus strains collectively were involved. And yet the incident is not without suggestive value. But the circumstances under which it was noted are so onerous that the observation is not likely soon to be repeated.

Beginning almost with the appearance of epidemic poliomyelitis in the United States in 1907, experimental studies were carried out at the Rockefeller Institute. A strain of human virus was implanted in rhesus monkeys. It was at first of low virulence, but a few passages enhanced its activity for the animals, and soon maximal virulence was attained and maintained by systematic inoculations for a term of three years. Then for wholly unknown reasons, diminution set in and the virus returned approximately to the low level of the original human material. Samples of the nervous tissues of infected monkeys had been regularly preserved in glycerol at +4° C., and these samples were retested from time to time to determine activity. About six years after the virus had diminished in infectivity, a rise in power was noted, and a second high level was attained about equalling the first. The enhanced virus has remained at that level during the past five years. Briefly, this specimen of virus passed through several distinct phases of activity: low, high, low, and again high, the last stage while specimens of nervous tissue were preserved in glycerol for several years without being subjected to animal passage.[12]

Certain epidemiologists, and notably Gotschlich, emphasizing the phylogenetic ascent of parasites from saprophytic bacteria, cite certain occurrences as indicating the transformation in nature of nonpathogenic into pathogenic organisms.[13] Such a supposed instance is that of Uhlenhuth and Zuelzer who, by employing animal passages, believed that they accomplished the conversion of a saprophytic water spiral into a pathogenic variety.[14] However, Neufeld,

an authority who favors the general point of view expressed, does not accept the interpretation given of this particular example.[15] Gotschlich, on the other hand, sees in the reappearance, after long cessation, of cholera in 1817 and of plague in 1894 in India, the operation of natural causes transforming the corresponding saprophytic into parasitic incitants of these diseases, a conclusion which with present knowledge will be acceptable to few bacteriologists. Neufeld among others urges that pandemics of influenza arise, not through successive distribution from one place to others of the highly virulent microbic incitant, but by reason of regional transformations of bacterial strains of low infectivity into strains of maximal virulence. That selected, more highly infective strains of pathogenic bacteria may be secured by animal passages is something pointed out by Pasteur and accomplished every day in the laboratory. But no experienced bacteriologist sees in this device the production of new or enhanced bacterial variants or species. The Germans, as do we, distinguish between mere separation or selection (*Auslese*) and modification (*Umstimmung*) by mutation or some other process of variation. Even as regards epidemic influenza, one cannot accept unqualifiedly the "local," as it may be termed, passage from low to high virulence of a microörganism, as accounting for the pandemics of that disease, seeing that outbursts follow lines of human travel, proceed in a geographical and chronological order, sweep past inaccessible communities, and show in general that characteristic to which the name "posting" has long since been applied.

Conscious of the inadequacy of the evidence adduced for the belief in microbic variation or mutation as accounting for the rise of epidemics, the protagonists of this view, as instanced by Neufeld, hold that support for it is to be sought in the appearance of new diseases. If it is admitted that the parasitic organisms have evolved from saprophytic ancestors, then at some period in history, the specific infections which have endured, must have emerged and presented themselves for the first time. It is, of course, entirely possible that none of our laboratory procedures suffices to initiate the transmutations involved. We should, therefore, be on the lookout for the occurrence of new types of infectious disease, incited by microörganisms not previously known. No one would, of course, wish to deflect this quest, or deny the possibility of a successful issue. A pertinent question just now would be whether epidemic

encephalitis may be regarded as a "new" disease. We are unfortunately in the weak position of not having discovered the incitant; and yet it is true that present-day internists and pathologists have had no previous experience of an epidemic disease of the nervous system corresponding to the multiform encephalitis. Even assuming that the incitant were actually isolated and proved wholly distinct from known pathogenic organisms, would the case for the "new" disease and the transformed parasite be proved? It may, I think, be doubted, in spite even of the incontestable fact that no such nervous disease had until recently come to the attention of physicians, and notwithstanding chronological relations to the recent pandemic of influenza, no corresponding epidemic disease attended the influenza outbursts of 1889 to 1892. Yet when the older records of epidemics, of which some certainly were and others might have been influenza, are searched as has been done so laboriously and interestingly by Crookshank, there are revealed associated occurrences of nervous or paralytic diseases to which one might hesitate to deny similarity with or relation to the epidemic encephalitis of the present time.[16] As one holding the view that epidemic influenza and epidemic encaphalitis are distinct entities, I wish nevertheless to put these facts before you. It cannot, moreover, be entirely without corroborative weight that although epidemic influenza ceased to prevail in this country in 1922–1923, yet epidemic encephalitis still marches on. The two diseases are surely not united specifically: whether they are engendered within a particular constitutional cycle, as Crookshank's argument implies, may be regarded as a hypothetical question which perhaps the experimentalist may ultimately be able to solve.

Let us, therefore, for the time being rest the case from the standpoint of human epidemic disease just here. If I have hurried you along rather breathlessly in epitomizing the present state of epidemiology, as ordinarily conceived, it is because I wish to lay before you a possible new mode of approach to some of its problems which, up to now, has been perhaps less invoked than it deserves. I refer to the study in relation to causes and effects of the epidemics occurring among animals to which we have ready access. Now all animals, even the most lowly, and plants of course, suffer from epidemic diseases. There is good reason for believing that in essential respects the happenings are comparable in all. Just the other day I read an account of an epidemic which swept through

and destroyed most of that devastating pest, the Mexican bean beetle—but not all—in one of the southern states. This imperfection of extermination is a characteristic of all epidemics, even the severest of man and animals. There is always a remnant of saving grace in the worst outbreaks.

The second or experimental part of this lecture deals with epidemics among mice and rabbits, the study of which has occupied us at the Rockefeller Institute for five years or more. I am led to report these studies in detail because I believe that they help us to comprehend better the events occurring in human epidemics. Doubtless in time epidemics among still other, perhaps still smaller animals, which can be numerously assembled, will come to be investigated. How far down the living scale we must go before we reach the limit of epidemics is not yet determined. Many of you know that d'Herelle, who has conducted remarkable investigations of the dissolving effects on bacteria of his so-called phage, conceives the active agent as a living virus—a kind of still smaller parasite within the bacteria affected. Although this happens not to be the generally entertained view of the undoubted phenomenon of bacterial autosolution, yet the event serves to recall the satiric lines of Swift, which I venture to quote in this connection:

> So, naturalists observe, a flea
> Has smaller fleas that on him prey;
> And these have smaller still to bite 'em;
> And so proceed *ad infinitum*.

## II.

In September, 1918, a spontaneous epidemic of mouse typhoid appeared in a breeding population of 2500 mice at the Rockefeller Institute and continued, with intervals of low death rate, for two and a half years during which time, through natural increase, the total numbers fluctuated between 1500 and 4000. The epidemic was followed closely, a mortality chart was kept, dead animals were autopsied systematically and occasional bacteriologic examinations were made. The epidemic finally ended, the cessation being hastened probably by systematic inoculation with killed cultures of the mouse-typhoid bacilli isolated from succumbing animals.[17] It was the timely occurrence of this epidemic which afforded the direct impulse to the experimental studies, still being

pursued, the outcome of which will now be presented.[18] It is, however, proper to record that our minds were receptive, ready, as one might say, to take advantage of this chance offering to study epidemics thus directly in animals, as the result of experiences with recent epidemic diseases in man.[19]

When the decision was made to attempt the experimental reproduction of epidemics of mouse typhoid, Amoss and I were not aware that a similar undertaking was well under way in England. Topley, whose investigations have been so fruitful, had already made a partial report in his Gulstonian Lectures which had just appeared in print.[20] Our plan differs somewhat in detail from the one Topley followed, for while Topley mingles infected and healthy mice introduced at intervals in large cages, Amoss and I set up a kind of mouse village in order to follow as closely as possible the spread of disease from cage to cage. In both instances the epidemics were started by feeding a small number of mice pathogenic cultures of a mouse-typhoid bacillus (enteritidis—paratyphoid group of bacilli). After a few days' interval or incubation a part of the fed mice developed and later succumbed to infection. To this source of disease healthy mice were exposed, either immediately, as in Topley's, or mediately, as in Amoss' and my experiments. We depended on the transfer of bacilli taking place through contamination of the hands of the attendant who fed the mice and cleaned the cages, very much as we suppose happens in spontaneous epidemics; it is interesting to note that no degree of mechanical or chemical disinfection sufficed to render the attendant's hands free of the bacilli.

In the half dozen years which have elapsed since the investigations have been under way there has been a good deal of parallelism between the experiments carried out by Topley, and Amoss, Webster, Pritchett and myself, and latterly by Neufeld and Lange, the actual results of which have been remarkably harmonious although the interpretations have not always coincided. There have also been differences in kind of experiment, according to the progress made in London or New York, and to the deductions separately based on the results obtained, as inevitably happens among experimenters and is conditioned by the particular imaginative outlook of one or another group of workers.[21] It is a pleasure to record that between the English and American investigators the best of feeling has always prevailed, and through correspondence and actual

visits the progress of events has been closely followed, and thus far without the slightest conflict and with common advantage all around.

It became immediately evident that it was possible to start continuing epidemics of typhoid among a healthy mouse village population, from which it was concluded that a wide, if not uniform, distribution of the bacilli was quickly effected by the attendant, leading to infection and death of some but not all the mice exposed. At the outset the number and distribution of deaths in the separate cages simulate the sporadic happenings noted often to precede the real epidemic outbreaks. This preëpidemic variety of the disease was later, as will appear, converted into a true epidemic prevalence, in which groups of mice sickened and died according to an order, suggesting, if only roughly at first, the periods or following waves of the spontaneous mouse epidemics, or epidemics as observed in man. The explanation of these events, observed by Topley in his single cage experiments and by us in the mouse village, was not at first wholly perceived. Topley ascribed them chiefly to rise and fall of bacillary infectivity, Amoss and I to fluctuations of virulence plus dosage of the bacilli. Later the discrepancies could be accounted for by Webster, who determined the interaction of three quite constant factors, namely, level of virulence of the bacilli, quality of resistance of the host or exposed mice, and quantity of bacilli ingested or dosage.[22]

To enable you to follow the succession closely, let me state that in Topley's experiments, once infection was started, fresh increments of healthy mice were placed in the cage at intervals. In Amoss' experiments, once a kind of equilibrium or stationary period of disease arose in the village, cages containing fresh, healthy mice were brought into contiguity with the previously exposed animals. In order to be brief, I will give you the bare results of a long series of observations of successive waves of mouse typhoid followed by recessions, thus induced, in which not only the new animals but the old or already exposed ones also were affected.

In three separate experimental attempts to induce outbreaks of mouse typhoid resembling the epidemic spread witnessed in breeding stocks and spoken of as arising spontaneously, the type of disease induced was first that of the sporadic prevalence, as shown by the number of mice dying and the number of cages attacked. Once, however, this state of sporadic disease is started in a mouse popu-

lation, all that appears necessary in order to convert the occasional deaths with low cage-attack rate into frequent deaths with high cage-attack rate, is to bring into contiguous relation with the infected population increments of not previously exposed healthy mice.[23]

The sporadic prevalence is quickly over. The new mice having been introduced, the succeeding events proceed in an orderly fashion. After an interval of about five days the latter, or new mice, begin to die, the number of deaths and the proportion of cages attacked rising day by day. During the first period in which the new mice fall victims to the disease the old mice do not show an increased death-rate. *But from the tenth to the twentieth day after the addition of the new mice, and hence the fifth to the fifteenth day following their deaths, the old mice are drawn into the wave of fatality, with the result that ultimately they suffer a mortality equal to or even greater than the new ones.*

The epidemics thus inaugurated, as indicated by the deaths, usually diminish or even disappear before all, sometimes after only a small part of the exposed mice have been destroyed. A tendency shown by all the experiments is for a state of equilibrium between the surviving mice and the infecting bacillus to be effected, this state continuing until fresh infectible material is provided, when there arise undulations or epidemic waves of deaths remarkably uniform in respect to the successive replacements of fresh mice. The undulations cease gradually, the late fatalities resulting not from delayed infection so much as from protracted illness and long survival. Bacillus carriers arise in the course of the epidemics and show, through possession of agglutinins, the existence of a partially immune state. It is through these carriers that the disease is propagated, in spite of which, as the events prove, the partially immune individuals are not themselves adequately safeguarded, since as we have seen, the older mice which have weathered one or more epidemic storms ultimately sicken and succumb. Here obviously another factor operates, and this all-important one in overcoming natural and acquired resistance is the factor of quantity or dosage of the bacilli.[24]

Topley, as already pointed out, and his predecessor, Danysz, considered fluctuation in virulence as the factor which chiefly determined the waves of epidemic prevalence of mouse typhoid, and Flexner and Amoss regarded the virulence plus dosage as the decid-

ing events. But it was the precise studies of Webster and Pritchett, on the constitution of the bacilli on the one hand and the reaction of the host on the other, which have yielded the constants with which to measure the actual happenings observed.[25]

We are, as one might say, in sore need of the simplification of the phenomena of the epidemic, which happily an accurate study of the living materials and other effective agencies seem capable of supplying. We need to measure not only bacilli and host, but such other factors as diet and season, if we wish to bring animal and human epidemic occurrences into harmonic relationship. Undoubtedly, certain of these extrinsic influences have been included in the term "telluric," as used by the older epidemiologists. Fortunately we may subject certain of the "influences" to experimental verification in order to introduce precision into our calculations, in opposition to such vague notions as "epidemic constitution." It would seem not inappropriate to introduce at this point of our discourse the significant words with which the young army surgeon, Helmholtz, as he was then, closes the introduction to the treatise giving to the world the mathematic physical demonstration of the conservation of energy, based in part, as you may recall, on physiologic studies carried out on voluntary muscle. He says: "Theoretical natural science, therefore, if she does not rest contented with half views of things, must bring her notions into harmony with the expressed requirements as to the nature of simple forces, and with the consequences which flow from them. Her vocation will be ended as soon as the reduction of natural phenomena to simple forces is complete, and the proof given that this is the only reduction of which the phenomena are capable."

With this ultimate purpose in mind we may now proceed to an analysis of the phenomena of mouse typhoid as experimentally induced in relation to such factors as constitution of bacilli, response of host and influence of dosage, diet and season, as determined by the precise studies of Webster and Pritchett upon homogeneous stocks of mice.

Bacilli were administered *per os* by means of a simple mechanical device, which delivered a fixed quantity, approximately 4,000,000 organisms, into the stomach. Five strains of enteritidis paratyphoid bacilli were tested on about 1400 mice. Stools and blood were studied by culture, and blood was tested for agglutinins. Three groups of mice were distinguished. In the first group the

bacilli disappear at once or after a brief period from the stools, and the blood is persistently negative for bacilli and agglutinins; the 20 to 30 per cent of mice composing this group continue well during the eight-week period of observation. In the second group the bacilli are passed for an irregular period; small numbers invade the blood and agglutinins are present and strong three weeks after the inoculation. The 5 to 10 per cent of the mice composing this group sicken but recover. The members of the third group pass large numbers of bacilli, many are cultured from the blood during life, and the 70 to 80 per cent of mice composing it sicken after five days' incubation and sooner or later die. The five bacillary strains differed among themselves in degree of virulence, but each one remained constant in its pathogenic action upon mice and was unaffected by animal passages. It could be shown, therefore, that the epidemic outbreak of greater or less severity of mouse typhoid is determined in large measure by inherent degree of bacillary virulence. An originally highly pathogenic strain is more destructive than an originally less active one, and antigenic identity is no measure of infective equivalence. In other words, the occurrence of two strains of the bacilli pathogenetically different and antigenically identical does not indicate transmutation of one into the other. When suitable tests are carried out by intraperitoneal inoculation the same general rules regarding virulence fixity of strains are found to apply.[26]

In order to determine the limits of the host response, the effect of varying dosage has first to be ascertained. When fixed quantities of cultures of given strains of mouse-typhoid bacilli are introduced into the stomach of mice of selected weight, and of the same lots as regards parentage and food, consistent results, as shown by the percentages of those surviving and succumbing, are obtainable. When massive doses of the bacilli are given the deaths fluctuate between 70 and 80 per cent; when critical doses are given the percentages vary from 40 to 50. When infection is permitted to take place by contact of inoculated with uninoculated mice the end-result is determined by the relative numbers of each kind in the combination. Thus when 5 inoculated mice are placed with 1 uninoculated animal the percentage mortality of the latter corresponds with that of the purposely inoculated, while when the ratio of inoculated to uninoculated is 1 to 1 the effect of the contact is very small.

These findings bring out two important points, namely, that

the susceptibility of a mouse population to mouse-typhoid infection is a relative or graded property; and that the dosage, as determined by the quantitative and spatial distribution of the bacilli, is a definite factor or constant, as shown by the mortality curve. A significant corollary to the findings is that irrespective of reasonable dosage and of strain of bacilli, from 20 to 30 per cent of mice ordinarily resist infection.

The statement just made regarding resistance indicates that using sufficient numbers of mice, the quality or degree of host susceptibility or resistance, according to the angle from which the results are viewed, may be found also to be a constant. Thus 540 mice of the same age and weight, bred at the Rockefeller Institute, were given *per os* a standard dose of culture of a mouse-typhoid bacillus. The mortality curves of the several tests were remarkably uniform. There were, it is true, minor variations which later, and as will appear, could be correlated with seasonal changes. The figures yielded by this large number of mice were employed to construct a so-called *standard control curve*, with which other curves could be profitably compared. For example, it was found that when mice were drawn from other sources and inoculated in an identical manner the curve differed from the standard one. Thus, mice procured from a Pennsylvania source yielded a curve lower than the standard, and mice from a New Jersey source, a curve exactly agreeing with the standard.[27]

This constancy of response among groups or stocks of mice to given strains and doses of the bacilli, suggested to Webster that after all the determining qualities residing within the animals might well be not of specific so much as of nonspecific nature, and something which comes into play, no matter what the nature of the poisonous agency may have been. With this idea in mind, he administered bichlorid of mercury also by stomach tube to groups of mice. It happened that with a dosage of 0.0033 gm. the mortality curve exactly parallels the standard curve. With larger and smaller doses of the drug curves are obtained reproducing those yielded by culture strains of higher and lower degrees of virulence.[27]

Up to this time the host material consisted of mice of common stocks, but not of pure-line origin. That heredity may affect the degree of susceptibility could be assumed. Fortunately, material was available to test this point directly, as was done by Pritchett. Two sets of experiments, extending over two years and involving

five separate strains of mice and 5000 individuals, were made. The strains consisted of three pure-line lots yielded by brother-sister matings and two homogeneous lots obtained by close inbreeding. During the first year 500 and during the second year from 300 to 600 mice of each strain were inoculated *per os* and closely followed. The result of this laborious study leaves no doubt that definite differences in susceptibility to typhoid exist among mouse stocks and that hereditary factors play an essential part in determining variations.[28]

Having now ascertained that the quality of the host plays a leading or decisive part in mouse-typhoid infection, it would seem to follow that the mice resisting bacterial infection should be the ones responding least to mercury bichlorid poisoning, as indeed was found by Webster to be the case. Moreover, he also found that when mice surviving ordinary lethal doses of mouse-typhoid bacilli are inbred for several generations, the offspring become progressively more resistant both to the bacilli and to mercury bichlorid; conversely, the offspring of females belonging to families of high susceptibility show the opposite tendency, and are less resistant to bacilli and chemicals than the corresponding unselected mouse material.[29]

With these data before us, we may turn for a brief consideration of certain of Topley's findings for which he gave no adequate explanation. It will be recalled that he assembled mice in large cages to which fresh animals were added at intervals. He found that when the additions were made in the period of decline of the epidemic the fresh mice were more likely to survive than when they were added at the ascent of the wave; also when the additions were made daily the deaths did not occur regularly, but came in waves nevertheless. Topley ascribed these happenings mainly to supposed fluctuation in virulence of the bacilli. We now know, thanks to Webster's accurate studies, that the bacilli do not so fluctuate, and we have also learned that host susceptibility and dosage of the bacilli largely affect infection and death. The probability, therefore, is that the wavelike movements, observed originally by Danysz and later by Topley and ourselves, in the course of mouse-typhoid epidemics are determined by the quantitative distribution or concentration of the bacilli acting on mouse populations previously unexposed or exposed. In all instances first the former and next the latter are affected, according to the measure of original

susceptibility and subsequent available quantity of bacilli. That this is the usual series of events was shown by Pritchett in a conclusive way. She devised means of estimating at two or three days' intervals the number of mouse-typhoid bacilli in a cage containing an infected population, to which daily additions of 2 healthy mice were made. The tests carried over a six-month period showed definitely that the mortality-rate rose regularly six to eight days after a large increase took place in the number of bacilli in the cage.[30]

Dosage of bacilli, therefore, in mouse typhoid—just as concentration in certain infectious diseases in man—is found to be a significant factor in initiating epidemics. It is well known that in order to diminish greatly, or even to abolish altogether malaria and yellow fever, we need not eliminate all the mosquito vectors; what is aimed at is to reduce the number to an established effective index, when the diseases disappear. When certain bacterial infections rage, streptococcus sore throat, for example, the number of carriers of hemolytic streptococci is large; as the malady abates, the number of carriers shrinks, and so with epidemic meningitis and other diseases. It is desirable that the fact be generally appreciated that in quantity of bacteria we have something which can break through the resistance barrier, be it natural or acquired. The persons vaccinated against smallpox or against typhoid fever, adequately protected under ordinary conditions of incidence of those diseases, may still be open to attack when the diseases become rampantly prevalent. The protective immunity mechanism is a measurable quantity, and may be superseded. When the quantity or dosage, so to speak, of the microbic assailant is large, and the grade of virulence high, even the extraordinary defenses of the body may prove insufficient.

We have now reviewed the inherent factors, microbe and host, as we may call them, as they react on each other, in the course of those happenings through which epidemics are generated. It will, I think, be admitted that the knowledge gained by the experimental method of study of the phenomena displayed by mouse typhoid is enlightening. In how far the data secured can be applied to other epidemic diseases and to hosts other than mice, has still to be determined. We know already, thanks largely to Webster's investigation of Bacterium lepisepticum infection in rabbits, that they are applicable to them.[31] But we have still to consider certain external or environmental influences which affect the course of

mouse typhoid and doubtless of other diseases as well. I shall deal, at this time, especially with the influence of food and of season on the course of mouse-typhoid infection.

That food should play a part in altering the course of an epidemic disease might perhaps be inferred from the profound effects produced by dietary deficiencies as expressed in beriberi, rickets, scurvy and possibly in pellagra. We shall deal, however, in this instance with no such extreme departures from the ordinary in diet. Indeed, it has been found—and just this is the surprising thing—that a diet to all intents and purposes adequate and favorable may nevertheless affect a stock of mice injuriously in comparison with another diet more ideally, as it seems, adjusted to their requirements.

Webster and Pritchett's experiments on food effects were simple in design. Two sets of mice were employed. One set was reared on the regular Rockefeller Institute ration in use for many years, and consisting of a daily feeding of baker's bread soaked in grade B pasteurized milk and warmed to 60° to 70° C., and supplemented by two weekly feedings of an oatmeal-buckwheat mixture and one weekly feeding of dog biscuit. The animals thrive and multiply on this diet. The diet with which this was compared was McCollum's normal one for rats and mice, consisting of wheat, 67.5 per cent; casein, 15 per cent; milk powder, 10 per cent; sodium chlorid, 1 per cent; calcium carbonate, 1.5 per cent; butter fat, 5 per cent. The mothers and the offspring, the latter being taken for experiment, were fed the McCollum mixture. Equal groups of mice fed on the two diets were given by stomach tube either about 4,000,000 mouse-typhoid bacilli or bichlorid of mercury. A very few of the mice were tested by intraperitoneal injection of 1 minimum lethal dose of botulinus toxin. The mice fed on the McCollum diet proved to be less susceptible to all three injurious agents. As the effect of the diet is directed against chemical as well as biologic poisons and in equal degree, we are justified in speaking of the defensive mechanism involved as nonspecific. This fact leads to the important conclusion that the factor which we so commonly invoke under the names of susceptibility or resistance is an innate quality of the host, brought into play under stress and strain of injury of widely various nature.[32]

Seasonal variations of disease are, of course, very well known. Even when we exclude those diseases which depend upon insect

vectors whose prevalence is determined by season, we still meet with examples which display strong seasonal fluctuations. The influence of season was tested on 5000 mice by Pritchett in two sets of experiments covering the twenty-four months' period from 1923 to 1925. A given number of mice, consisting of three pure-line and two homogeneous strains, was inoculated by stomach tube every month with about 5,000,000 mouse-typhoid bacilli of fixed virulence. Each test was run for eight weeks, the deaths being recorded daily and routine bacteriologic examinations being carried out. Not only were seasonal variations displayed, but they were remarkably uniform over the two twelve months' periods; yet certain, if slight exceptions arose. As the mouse material was by heredity of heterogeneous nature, certain differences in response to infection resulted from that circumstance. And yet it may be stated that the course of events was uniformly such that the mortality curves tended to arrange themselves into three series, namely, curves indicating: (*a*) High spring mortality; (*b*) low summer mortality; (*c*) intermediate fall and winter mortality. Expressed in terms of deaths, we may say that the spring rate is high, the summer rate low and the fall and winter rate, while falling between the two, may in the early fall rise sharply and even approximate the spring level. Since, however, the seasons, year by year, are only roughly comparable and vary in temperature, sunlight and other conditions week by week or month by month, a certain amount of fluctuation in the curves is to be expected, provided that it is affected, as it appears to be, by meteorologic occurrences.[33]

It would be desirable, in view of recent discoveries of the profound effect of light in protecting the animal organism from rickets through its influence on the calcium metabolism, to study the part which it may play in epidemics. Indeed, the recent precise studies of Brown and Pearce on the effects of sunlight, especially on the normal as well as on the pathologic organism, already point to important correlations. They have secured data from 400 normal rabbits, observed month by month over a period of three years, and a like number of rabbits inoculated with a malignant tumor and with syphilis, similarly studied. They have found first that, contrary to current belief, no fixed relation of size and weight attaches to the individual organs, but that the relationships are constantly changing in a more or less rhythmical manner. Hence what might be regarded as normal at one time would be regarded as abnormal at

another time. The weights of the heart, liver, kidneys, and even the brain in proportion to body weight, fluctuate in the course of a year as much as 20 to 40 per cent; while the endocrine organs, lymph nodes and spleen show variations of 50 to 100 per cent. Constant readjustments of the relative balance among the various organs of the body takes place, and this system of changes follows a regular course which may be correlated with the seasonal changes of the year. So far the meteorologic condition which occupies the place of most importance is sunlight. Just as the organs increase and diminish in relative size, so it appears do the severity of the tumor and the manifestations of syphilis in the rabbit rise and fall according to the organic changes. From this it may be inferred that the seasonal variations affect functional activity in that they coincide with or induce alterations of the state of the animal body with which pathologic effects are related.[34]

We have now arrived at a natural halting place in this discourse, from which to view the ground that has been covered. We may, I believe, discern a certain order and sequence of events in determining epidemic occurrences in at least one infectious disease in animals. Not only may the origin of the mouse-typhoid epidemic be accounted for by the presence of the offending bacillus, but the course pursued is, as it were, predictable on the basis of the constitution of microbe and host, as affected by such modifying causes as dosage and particular environmental conditions. The preponderant rôle of dosage and fresh infectible host material is clearly indicated in prolonging the epidemic and explaining the periodic wavelike movements. That the spontaneous epidemics of mice are prolonged in an identical manner by new births and by the spatial and quantitative distribution of bacilli may be assumed as quite certain. Application of these findings to the study of epidemics of human diseases in which more precise observation shall take the place of actual experiment is the possibility clearly indicated. Perhaps in this manner will the next forward step be taken leading to the solving of riddles in epidemiology as related to man.

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11. Neufeld, F.: Centralbl. f. Bakteriol., Parasitenk. u. Infektionskr., Orig., Abt. 1, 1924, p. 93. Morgenroth, J.: Centralbl. f. Bakteriol., Parasitenk. u. Infecktionskr., Orig., Abt. 1, 1924, p. 94. Falk, J. S., and Jacobson, M. A.: J. Infect. Dis., 1925, xxxvii, 507. Jordan, E. O.: J. Am. Med. Assn., 1926, lxxxvi, 177.

12. Flexner, S., Clark, P. F., and Amoss, H. L.: J. Exper. Med., 1914, xix, 195.

13. Gotschlich, E.: In Rubner, M., v. Gruber, M., and Ficker, M.: Handb. d. Hyg., Abt. 1, 1913, iii, 199.

14. Uhlenhuth and Zuelzer: Centralbl. f. Bakteriol., Orig., Abt. 1, 1921, lxxxv, 141.

15. Neufeld, F.: Loc. cit.

16. Crookshank, F. G.: Loc. cit.

17. Lynch, C. J.: J. Exper. Med., 1922, xxxvi, 15.

18. Flexner, S. and Amoss, H. L.: Proc. Nat. Acad. Sci., 1921, vii, 319.
Flexner, S.: J. Exper. Med., 1922, xxxvi, 9.
Amoss, H. L.: J. Exper. Med., 1922, xxxvi, 25, 45.

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21. Webster, L. T.: Am. J. Hyg., 1924, iv, 134; 1925, v, 335.
Greenwood, M., and Topley, W. W. C.: J. Hyg., 1925, xxiv, 45.
Neufeld, F.: Klin. Wchnschr., 1924, iii, 1345.

22. Topley, W. W. C.: Lancet, 1919, ii, 1, 45, 91.
Webster, L. T.: J. Exper. Med., 1923, xxxvii, 231, 269.

23. Amoss, H. L.: J. Exper. Med., 1922, xxxvi, 45.

24. Flexner, S.: J. Exper. Med., 1922, xxxvi, 9.
Webster, L. T.: J. Exper. Med., 1923, xxxvii, 269.

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Topley, W. W. C.: Lancet, 1919, ii, 1, 45, 91.
Webster, L. T.: Am. J. Hyg., 1924, iv, 134.

26. Webster, L. T.: J. Exper. Med., 1923, xxxvii, 231, 781; xxxviii, 33, 45.

27. Webster, L. T.: J. Exper. Med., 1923, xxxvii, 231; xxxviii, 45.

28. Pritchett, I. W.: J. Exper. Med., 1925, xli, 195; 1926, xliii, 161.

29. Webster, L. T.: J. Exper. Med., 1924, xxxix, 129, 879; 1925, xlii, 1.

30. Pritchett, I. W.: J. Exper. Med., 1926, xliii, 143.

31. Webster, L. T.: J. Exper. Med., 1924, xl, 117.

32. Webster, L. T., and Pritchett, I. W.: J. Exper. Med., 1924, xl, 397.

33. Pritchett, I. W.: J. Exper. Med., 1925, xli, 209; 1926, xliii, 173.

34. Pearce, L., Brown, W. H., and van Allen, C. M.: J. Exper. Med., 1924, xl, 603; Proc Soc. Exper. Biol. and Med., 1924, xxi, 371, 373.

## ANNUAL REPORT OF THE LIBRARY COMMITTEE FOR 1925

Mr. President: In accordance with the ordinances and By-Laws of the College, I herewith submit the following report of the Library Committee for the year 1925:

| | |
|---|---|
| Total number of volumes in the Library, including the bound volumes and 21,493 unbound "Reports" and "Transactions" | 146,998 |
| Number of unbound "Theses" and "Dissertations" | 24,393 |
| Number of unbound Pamphlets | 148,958 |

Included in the above are 4248 volumes known as "Reserves," consisting of second copies of some of the more important periodical publications; also 2860 volumes more or less incomplete.

The duplicates, which number 1475 at this date, are not included in the above total.

The following table shows the number of volumes in the various divisions of the Library:

| | Bound. | Incomplete and unbound. | Total. |
|---|---|---|---|
| General Library | 104,686 | 2,860 | 107,546 |
| Lewis Library | 13,787 | 44 | 13,831 |
| On permanent deposit: | | | |
| S. D. Gross Library | 3,718 | 3 | 3,721 |
| Library of the Obstetrical Society of Philadelphia | 217 | 0 | 217 |
| Mütter Museum* | 190 | 0 | 190 |
| | | | 125,505 |

Received during the year, from all sources, 3627 volumes, 8222 pamphlets and 11,732 numbers of various periodicals.

* The books of the Mütter Museum are not permitted to be removed from the College building.

Divided as follows:

| | Volumes. | Pamphlets. | Journals |
|---|---|---|---|
| General Library | 3,202 | 7,969 | 11,337 |
| Lewis Library | 17 | | |
| S. D. Gross Library | 5 | | |
| By purchase, General Account | 150 | | |
| In exchange | 253 | 253 | 395 |
| | 3,627 | 8,222 | 11,732 |

Accessions (including 34 volumes of "Reserves"): 2417.

| | Volumes |
|---|---|
| General Library | 2,394 |
| Lewis Library | 17 |
| S. D. Gross Library | 5 |
| Mütter Museum | 1 |
| | 2,417 |

Total increase in the number of volumes for the year, 2417.

Photographs received in response to requests sent out during the past year and voluntary gifts: Fellows of the College, 2; other than Fellows, 35.

Total number of portraits listed, 11,404.

The individual "Donors" for the year ending November 1, 1925, number 451; this represents 991 distinct presentations. Each gift is duly acknowledged.

The following list shows individual gifts of more than 25 volumes; also the number of volumes presented by the various publishing houses:

| | Volumes. |
|---|---|
| Dr. Joseph Leidy | 301 |
| Dr. Morris J. Lewis | 269 |
| Dr. William J. Taylor | 177 |
| Mrs. E. A. Cálves | 118 |
| Dr. John H. W. Rhein | 81 |
| Dr. E. A. Shumway | 68 |
| Dr. Thomas C. Kelly | 58 |
| Dr. DeForest P. Willard | 36 |
| Dr. E. E. Montgomery | 35 |
| Dr. Hobart A. Hare | 34 |
| Dr. Charles K. Mills | 31 |
| Dr. Francis R. Packard | 30 |
| Mrs. John B. Roberts | 28 |
| Dr. George W. Norris | 26 |

From the publishing houses of:

| | Volumes. |
|---|---|
| P. Blakiston's Son & Co. | 23 |
| F. A. Davis Company | 17 |
| Lea & Febiger | 15 |
| J. B. Lippincott Company | 24 |
| W. B. Saunders Company | 49 |

The Library is indebted for large gifts of pamphlets and unbound periodicals to the following donors:

Dr. Astley P. C. Ashhurst
Dr. John Aulde
Dr. Charles W. Burr
Dr. Burton Chance
Dr. J. M. Cruice
Dr. Warren B. Davis
Dr. W. A. Newman Dorland
Dr. Alfred Hand
Dr. Hobart A. Hare
Dr. Addinell Hewson
Dr. Charles Judson
Dr. W. W. Keen
Dr. E. B. Krumbhaar
Dr. Morris J. Lewis
Dr. Edward Martin
Dr. Charles K. Mills
Dr. John H. Musser
Dr. George W. Norris
Dr. Charles J. O'Reilly
Dr. Maurice Ostheimer
The Pennsylvania Hospital
Dr. John H. W. Rhein
Dr. George E. de Schweinitz
United States Public Health Service
Dr. J. J. Walsh
Dr. A. C. Wood

690 new publications were added to the Library during the past year, viz.: United States, 313; Great Britain and Colonies, 222; France, 39; Germany, 94; Italy, 3; all other countries, 19. Of these new publications, 25 were written or edited by Fellows of the College.

25 volumes were presented by the following authors or editors:

Dr. John Alexander
Dr. Emmons R. Booth
Dr. Lloyd V. Briggs
Dr. Gordon Cameron
Dr. George W. Crile
Dr. Arthur F. Coca
Dr. Thomas S. Cullen
Dr. Eldridge L. Eliason
Dr. Claudio Fermi
Dr. Evarts A. Graham
Dr. Robert L. Graham
Dr. Hobart A. Hare (Editor)
Dr. Henry R. Harrower
Dr. Philip Horowitz
Dr. William H. Howell
Dr. Hugh M. Kinghorn
Dr. John A. Kolmer
Mr. John F. Lewis
Mr. Jesse G. Munsell
Dr. Ludwig A. Nékám
Dr. Joseph A. Rivière
Dr. Lee Alex. Stone
Dr. Benjamin White

18 volumes were sent by the publishers at the request of the following authors or editors:

Dr. Lewellys F. Barker
Dr. Stuart Close
Dr. Leroy Crummer
Dr. Harvey Cushing
Dr. Francis X. Dercum
Dr. Clifford B. Farr
Dr. Burton B. Grover
Dr. Hobart A. Hare
Dr. Chevalier Jackson
Dr. Walter A. Jayne
Dr. Thomas McCrae
Dr. Michael V. O'Shea
Dr. Henry L. K. Shaw
Miss Susan P. Wharton (compiler)

Summary of the "Funds:"

| | Volumes purchased. | Cost. |
|---|---|---|
| Henrietta Rush Fales Baker Fund | 52 | $294.95 |
| Luther S. Bent Fund | 40 | 115.84 |
| William T. Carter Fund | 18 | 17.46 |
| Gerardus Clarkson Fund | 24 | 81.38 |
| Francis X. Dercum Fund | 43 | 164.89 |
| Louis A. Duhring Fund | 55 | 371.42 |
| John D. Griscom Fund | 118 | 475.22 |
| William F. Jenks Fund | 92 | 494.93 |
| Oliver A. Judson Fund | 17 | 67.91 |
| William V. and John M. Keating Fund | 11 | 62.85 |
| William W. Keen Fund | 89 | 488.01 |
| Library Endowment Fund | 146 | 618.84 |
| Horace Magee Memorial Fund | 123 | 579.02 |
| J. Ewing Mears Fund | 37 | 70.51 |
| Charles K. Mills Fund | 2 | 2.68 |
| Weir Mitchell Fund | 97 | 160.95 |
| E. E. Montgomery Fund | 8 | 36.07 |
| John H. Musser Fund | 11 | 40.36 |
| Elizabeth K. Newcomet Fund | 14 | 35.32 |
| William F. Norris Fund | 41 | 413.69 |
| Charles A. Oliver Fund | 13 | 38.09 |
| Philadelphia Medical Society Fund | 7 | 86.80 |
| Lewis Rodman Fund | 60 | 152.25 |
| Douglas Stockton Warren Fund | 25 | 133.05 |
| John F. Weightman Fund | 44 | 281.49 |
| Caspar Wistar Fund | 48 | 309.23 |
| | 1,235 | $5,593.21 |

Special accounts:

| | | |
|---|---|---|
| Fund for completing files of journals | 111 | $471.31 |
| Fund for rare and valuable books | 38 | 306.76 |
| S. D. Gross Library Account | 2 | 25.55 |
| | 151 | $803.62 |

| | Expended. |
|---|---|
| Catalogue Endowment Fund—On account of salaries . . | $31.50 |
| Louis A. Duhring Fund—General Purposes of the Library . | 10,000.00 |
| Morris Longstreth Library Fund—On account of salaries . | 961.98 |
| George B. Wood Fund—Library supplies, stationery, etc. . | 327.02 |

Number of volumes bound, 848.

| | Visitors. | Fellows. | Total. |
|---|---|---|---|
| Use of the Library . . . . . | 5,397 | 1,853 | 7,250 |

The Library has been kept open two evenings each week and on the six minor legal holdays, for the same hours and period of time, as during the past year:

| Evenings. | Visitors. | Fellows. | Total. |
|---|---|---|---|
| 76 . . . . . | 625 | 207 | 832 |

| Legal holidays. | Visitors. | Fellows. | Total. |
|---|---|---|---|
| 6 . . . . . | 60 | 23 | 83 |

These figures are included in the total given for the year.

| | 1925. | 1924. | Increase. |
|---|---|---|---|
| Number of volumes consulted in the Library . . . . . | 23,512 | 13,521 | 9,991 |

The number of books "consulted in the Library" includes only those supplied on demand. Readers have access to the bound volumes and works of reference kept on the shelves in the Reading Room and the Fellows of the College have access to the Book Stacks. There are, therefore, a large number of volumes consulted of which no accurate record can be kept.

Number of volumes taken out:

| 1925. | 1924. | Increase. |
|---|---|---|
| 4,606 | 4,313 | 293 |

Use of Study Rooms: Average number of rooms in use throughout the year, 5. Greatest number in use at one time, 7. Daily average of the number of volumes in use in these rooms, 158.

Cataloguing:

| | Works. | Volumes. | Cards. written. | Printed cards revised. |
|---|---|---|---|---|
| Cataloguing . . . | 1,053 | 1,132 | 4,823 | 2,544 |

All books added to the shelves during the past year and 302 of the more important pamphlets have been catalogued and shelf-listed; and all bound volumes, including periodicals, transactions and reports, have been accessioned.

Revision of the Catalogue: 5794 cards have been revised, rewritten and filed.

4736 unbound pamphlets and reprints have been subject-headed and arranged alphabetically by subject and by author under the subject. It is expected that the binding of the pamphlets by subjects will be started in the coming year.

We have listed November 1, 1925, 1221 current periodical publications, including "Transactions" and "Reports" obtained through the following sources:

| | American. | Foreign. |
|---|---|---|
| Endowment Funds | 81 | 383 |
| By purchase from General Account | 39 | 159 |
| In exchange | 58 | 111 |
| Editors | 81 | 13 |
| Publishers | 40 | 16 |
| In addition, current numbers of periodicals have been received, at stated intervals, through the courtesy of the Editor of the *Therapeutic Gazette* | 39 | 46 |
| | 338 | 728 |
| Reports, not included in the above | 140 | 15 |
| | 478 | 743 |

The actual number of periodicals received during the year, including new subscriptions (4 American, 19 Foreign) total 1066. This is an increase of 31 over the previous year.

The following is a list of the foreign schools of medicine with which we exchange publications at the present time:

University of Amsterdam
" Basel
" Berlin
" Bonn
" Breslau
" Geneva
" Giessen
" Göttingen
" Halle
" Heidelberg
" Kiel
University of Königsberg
" Lausanne
" Leiden
" Leipzig
" Liège
" Lund
" Marburg
" Rostock
" Strassburg
" Upsala
" Utrecht
University of Würzburg
Faculty of Medicine of Paris
Faculty of Medicine of Toulouse

During the past year we have heard from Amsterdam, Basel, Berlin, Bern, Breslau, Erlangen, Giessen, Göttingen, Heidelberg, Kiel, Königsberg, Lausanne, Leiden, Leipzig, Marburg, Paris, Upsala and Utrecht. 1809 dissertations and 824 theses have been added to our collection.

We have received in cash from the sale of duplicates for the current year ending November 1, 1925, $1246.97.

This includes the sale authorized by the Library Committee, October 27, 1924, that the entire collection of duplicates be sold to the Medical School, University of Otago, Dunedin, New Zealand, for the formation of a Library, at the nominal price of ten cents per volume. There were 11,310 volumes and the amount received was $1131.00. While the duplicates have been disposed of in bulk for a similar purpose, a number of times during the past forty years, this is the largest single transaction in the history of the Library. It must, of course, be understood that during the period these duplicates were accumulating, exchanges were made each year with various other libraries, and in addition, the books were open for inspection and quite a number of volumes disposed of to individuals.

During the past year we have distributed books and journals, on exchange account to the following:

Academy of Medicine, Toronto
Boston Medical Library
Columbia University
Liverpool School of Tropical Medicine
Medical Society of the County of Kings, Brooklyn

and have received exchanges from:

Academy of Medicine, Toronto
Boston Medical Library
Columbia University
Liverpool School of Tropical Medicine
Medical Library Association, Baltimore

With the aid received from exchanges and purchases made with funds appropriated for the purpose by the Library Committee, we have been able to complete the files of the following journals:

Der ärtzliche Praktiker, Hamburg und Berlin
Archives Neederlandaises de Physiologie de l'Homme et des Animaux, La Haye
Nordiskt Medicinskt Arkiv, Stockholm
Lo Sperimentale, Firenze

Amount of fines collected for the current year ending November 1, 1925, $102.55.

List of rare medical books and works of special interest received during the year (it must of course be understood that these rare books, what may be termed medical classics, have been acquired without in any way interfering with the purchase of current medical publications):

### Incunabula

(Total number of incunabula at this date, 367 Titles, 351 Volumes.)

Averrhoes Cordubensis: Destructiones destructionum.*** Venetiis, Octavianus Scotus, Modoetiensis per Bonetum Locatellum, Presbyter Bergomensis, 1497.

Presented by E. B. Krumbhaar, M.D.

Bossus, Matthaeus: De institvendo sapientia animo. Bononiae, Plato de Benedictus, Bononiensis, 1495. [Hain 3677.]

[*ff.* 127–128 *missing supplied mss.*]

Fund for Rare Books.

Guarinus [Vocabularius breviloquus]. Basileae [Johannes de Amerbach] 1478. [Copinger II, 6285.]

Fund for Rare Books.

### *Works of Special Interest*

Aitken, John. Systematic elements of the theory and practice of surgery. Edinburgh, Gordon, 1779.

Presented by Miss Margaret O'Hara.

Allen, Charles. Curious observations on the teeth; the first known work on dentistry in the English language, with a short introduction by L. Lindsay. London, Bale, 1687. [Repr. 1924.]

[*Title-page fac-sim.*]

Luther S. Bent Fund.

Aristoteles. Secreta secretorum Aristotelis. Parisiis, 1520.

William T. Carter Fund.

Bell, Benjamin. Cours complet de chirurgie théorique et pratique. Traduit de l'Anglois par E. [F. M.] Bosquillon. 3 éd. Paris, Barrois, an IV [1796].

Presented by T. C. Crandall, M.D.

Bevilacqua, Francesco. Trattato nuova de' cancri in cui con tale occasione si discorre degli scirri, carcinomi, polipi, scrofole, fistole, ed altri tumori pertinaci, è mali di cura difficile, che vengono in ogni parte del corpo umano. Tradotta dalla lingua Francese. Venezia, Appresso Guiseppe Corona, 1742.

Fund for Rare Books.

Brandelius, Laurentius. De sensibilitato ossium morbosa, pro gradu doctoris disputabit. Upsaliae, apud John Edman, 1780.

Fund for Rare Books.

Cocchi, Antonio. Dei bagni di Pisa trattato. Firenze, nella stamperia imperiale, 1750.

Fund for Rare Books.

Cocchi, Antoni. Discorso primo. Sopra Asclepiade. Firenze, Albizzini, 1758.

John D. Griscom Fund.

Denys, Jacobus. Observationes chirurgicae de calculo renum, vesicae, urethrae, lithotomia et vesicae punctura, in quibus lithotomiae methodum, quam celeberrimus Joannes Jacobus Rau.*** Lugduni Batavorum, apud Joannem à Kerckhem, 1731.

Fund for Rare Books.

Dercum, Laurentius Antonius. Dissertatio inauguralis medica physiologica-anatomica exhibens theoriam nervorum.*** Wirceburgi, typis Joannis Jacobi Christophori Kleyer, 1737.

[*Photostat copy.*]

Presented by Francis X. Dercum, M.D.

Dercum, Laurentius Antonius. Hercules Lernaeae Hydrae domitor, parallelo carmine decantatus.*** [Verses chanted or sung on the occasion of conferring diplomas [honorary degrees?] upon L. A. Dercum and V. J. Grill.] Wirceburgi, typis Joannis Jacobi Christophori Kleyer, 1738.

[*Photostat copy.*]

Presented by Francis X. Dercum, M.D.

Desforges, Estienne. Les principes de la chirurgie, reduits par tables, avec leurs explications en faveur des aspirans audit art. Paris, l'Autheur, 1673.

Fund for Rare Books.

Du Hamel, Joannes Baptista. Regiae scientiarum Academiae historia, in qua praeter ipsius Academiae originem et progressus, variasque dissertationes et observationes per triginta quatuor annos factas, quàm plurima experimenta et inventa, cùm physica, tum mathematica in certum ordinem digeruntur. Secunda editio. Parisiis, apud Joannem-Baptistam Delespine, 1701.

Fund for Rare Books.

Eglinus, Iconius Raphael. Cheiragogia heliana philosophico necdum cognito.*** Marpurgi Cattorum, ex off. Rudolphi Hutvvelckeri, 1612.
Fund for Rare Books.

Forestus Alcmarianus, Petrus. Observationum et curationum medicinalium libri tres, nempe tertius de febribus intermittentibus; quartus de hecticis; ac quintus de febribus compositis.*** Antverpiae, apud Christophorum Plantinum, 1586.
Fund for Rare Books.

Franks, John. Observations on animal life, and apparent death, from accidental suspension of the function of the lungs with remarks on the Brunonian system of medicine. London, Reynell, 1790.
Presented by The Pennsylvania Hospital.

Galen, Claudius. De arte curativa ad Glauconem libri duo, Nicolao Leoniceno interprete. 2 Vols. in 1. Parisiis, Colinaeus, 1528.
Fund for Rare Books.

Galen, Claudius. De curandi ratione per sanguinis missionem, liber; eiusdemque de hirudinibus, reuulsione, cucurbitula et scarificatione libellus Theodorico Gerardo Gaudano interprete. Quibus cum edidimus de venae sectione aduersus Erasistratum librum, et libru aduersus Erasistrataeos qui Romae degebant Iosepho Tectandro Cracouoensi interprete. Lvgdvni, apud Gulielmum Rouillium, sub scuto Veneto, 1549.
Fund for Rare Books.

Galen, Claudius. (Galeni pergameni.) De naturalibus facultatibus libri tres. De pulsuum usu liber unus item et quaedam Pauli Aeginetae, de diebus criticis Thoma Linacro Anglo interprete. 3 Vols. in 1. Parisiis, apud Simoneum Colinæum, 1528.
Fund for Rare Books.

Gatti [Angelo]. Réfléxions sur les préjugés qui s'opposent aux progrés et à la perfection de l'inoculation. Bruxelles, Musier, 1764.
Presented by James Penniman, Esq.

Gautier d'Agoty, Arnaud Eloy. Cours complet d'anatomie point et gravé en coleurs naturelles. Nancy, Leclerc, 1778.
Fund for Rare Books.

Glass [Thomas]. Letter to [George] Baker on the means of procuring a distinct and favourable kind of small-pox, and on the use of cold air and cold water in putrid fevers. London, Johnston, 1767.
Horace Magee Memorial Fund.

Gramm, Caeso. Disputatio philosophica de monsteris eorumque causis atque differentiis.*** Basileae, Typis Georgii Deckeri, 1640.
William F. Jenks Fund.

Helvetius, Johannes Fridericus. Microscopium physiognomiae medicum, id est, tractatus de physiognomia.*** Amstelodami, Waesbergios, 1676.
Fund for Rare Books.

Hippocrates. [Opera.] Hippocratis Coi medicorvm omnivm longe principis, octoginta volumina, quibus maxima ex parte, annorum circiter duo millia Latina caruit lingua, Graeci uero, Arabes***nunc tandem por M. Fabium Caluum Rhauennaten latinitate donata.*** Romae, ex aedibus Francisci Minitii Calvi, 1525.
Presented by Charles W. Burr, M.D., and E. B. Krumbhaar, M.D.

[Horneck.] The high German doctor; to which is added, a large appendix, with an explanatory index. 2 Vols. London, Baker, 1715–1719.
Presented by A. P. C. Ashhurst, M.D.

Hornius, Christophorus. De avro medico philosophorum; id est de illo occulto salutari, solari omnium mineralium, vegetalium, et animalium corporum, spiritu, seu balsamo, viuifico, et maxume alexiterio, bezoartico, theriacali.*** Francofurti, typis Wolffgangi Richteri, 1615.
Fund for Rare Books.

Icones stirpium seu plantarum tam exoticarum, in gratiam herbariae studiosorum in duas partes digestae. Cum septem linguarum indicibus, ad diuersarum nationum usum. 2 Parts in 1 Vol. Antverpiae, ex officina Platiniana, apud Viduam et Ioannem Moretum, 1591.
Fund for Rare Books.

James, Robert. New method of preventing and curing the madness caused by the bite of a mad dog. London, Osborne, 1743.
Fund for Rare Books.

Kalid Rex. Liber secretorum; siue, Lapidis philosophici secreta secretorum ***traduntur ex Hebraeo primum in Arabicum, et demum in Latinum traducta.*** Francofurti, Bringeri, 1615.
Fund for Rare Books.

Leonicenus, Nicolaus. Opuscula nuper in lucem aedita quorum nomina proxima habentur pagella. Venetiis, Bernardinus Vitalis, 1525.
Caspar Wistar Fund.

Malovin. Della malattia del moccio de'cavalli detta volgarmente morva observazioni, ed esperienze del *** precedute da un discorso del Signor di Buffon, e da alcuni articoli estratti dall'opera del Sig. La-Fosse intitolata Guida del maniscalco. Tradotto dal Francese. Torino, Fratelli Reycends Mercanti libraj sul Cantone di contrada nuova vicino a Piazza Castello, 1768.
Fund for Rare Books.

Marten, John. Gonosologium novum; or, A new system of all the secret infirmities and diseases, natural, accidental, and venereal in men and women.*** 6 Ed. London, Crouch, 1709.

Fund for Rare Books.

Mauriceau, François. Traité des maladies des femmes grosses.*** Nouvelle edition. Geneve, Dentant, 1693.
[*Engraved title-page.*]

William F. Jenks Fund.

Novae Academiae Florentinae opuscula aduersus Auicennam, et medicos neotericos, qui Galeni disciplina neglecta, barbaros colunt.*** Venetiis, Juntae, 1533.

Lewis Rodman Fund.

Pulverinus, Joannes Hieronymus. De curandis, iuxta hodiernum usum, singulis humani corporis morbis, opus, sive praxis accurata brevi, dilucida et absoluta methodo explicata, ac tradita.*** Venetiis, apud Iac. Ant. Somaschum & Paulum Venturinum, 1600.

Henrietta Rush Fales Baker Fund.

Rathlauw, Jan Pieter. Practical observations on the insufficiency of the common methods of treating many diseases of the human body.*** London, Printed for the Author, 1769.

By Purchase.

Reichel, Joannes Andreas. Sistens theoriam haemoptoes.*** Erfordiae, Heringii, 1737.

Fund for Rare Books.

Ridley, H. Anatomy of the brain, containing its mechanism and physiology together with some new discoveries and corrections of ancient and modern authors upon the subject.*** London, Smith, 1695.

Presented by Walter Roberts, M.D.

Riedlin, Veit. Iter medicum sanitatis recuperandae causa non solum institutum.*** Augustae Vindelicorum, apud Laurentium Kronigerum et Haerdes Theophili Goebeilii, typ. Abrahami Guggeri, 1702.

Douglas Stockton Warren Memorial Fund.

Rowley, William. Treatise on female, nervous, hysterical, hypochrondriacal, bilious, convulsive diseases.*** London, Nourse, 1788.

Presented by the Pennsylvania Hospital.

à Roy, Corn[elius] Henr[icus]. Commentatio anatomico-chirurgica de scoliosi. Lugduni Batav.; apud F. R. de Does, 1774.

Fund for Rare Books.

Ryan, John. Commentary on the dysentery; or, bloody flux. Translated from the Latin of Mark Akenside. London, Noble, 1767.

Presented by The Pennsylvania Hospital.

Schreyer, Johannes. Trinum fluidum magnum seu natura aquae, vini et cerevisiæ, accommodata ad tres cizensibus maxime usuales liquores, aquam, vinum et cerevisiam. Ciza, typis Hetstedianis Cizensibus, 1687.

Fund for Rare Books.

Simmons, Samuel Foart. Practical observations on the treatment of consumptions. London, Murray, 1770.

Presented by the Pennsylvania Hospital.

Squire, Samuel. Sermon preached before his Grace Charles, Duke of Marlborough, president, the vice-presidents, the treasurer, etc., of the hospitals for small-pox, on Thursday, March 27, 1760. London, Woodfall, 1760.

Horace Magee Memorial Fund.

Templeman, Peter. Curious remarks and observations in physics, anatomy, chirurgery, chemistry, botany and medicine. Extracted from the history and memoirs of the Royal Academy of sciences at Paris.*** 2 Vols. London, Davis, 1753–1754.

By Purchase.

Vicq-d'Azyr, Félix. Oeuvres de Félix Vicq-d'Azyr, recuellies et publiées avec des notes et un discours sur sa vie et ses ouvrages, par J. L. Moureau. 6 Vols. Paris, Duprat-Duverger, an XIII [1805].

Fund for Rare Books.

Vieussens, Raymond. Deux dissertations; la premier, Touchant l'extraction du sel acide du sang; la seconde, Sur la proportion de quantité de ses principes sensibles. Montpellier, Pech, 1698.

Caspar Wistar Fund.

Wimpineus, Joh. Albertus. De concorda Hippocraticorum et Paracelsistarum libri Magni excursiones defensivae, cum appendice, quid medico sit faciendum. Argentinae, par Carolum Kieffer, 1615.

Fund for Rare Books.

*Manuscripts*

Alumni Association of the Jefferson Medical College. Minutes of the meetings. 1886–1896.

Presented by Stricker Coles, M.D.

Bill presented to the Senate and House of Representatives of Pennsylvania, December 29, 1810, recommending laws pertaining to the Practice of Medicine, signed by Benjamin Rush, Caspar Wistar, Jr., Benjamin S. Barton, Philip Syng Physick, John S. Dorsey, and John Redman Coxe.

Presented by the Descendants of the late Nicholas Biddle, Esq., through the courtesy of Mr. Edward Biddle.

Cameron, Gordon. Pancreatic anomalies; their morphology, pathology and clinical history, Victoria, 1924.

[*Typewritten manuscript.*] (*Alvarenga prize essay.*)

Presented by the Author.

Harvey, William. Transcript and photostat negative of a letter written probably in the year 1631 to Viscount Dorchester, at that time principal secretary to King Charles 1st.*** preserved in the Bodleian library at Oxford amongst the Clarendon papers. No. 2076 and was published by J. H. Aveling in his "Memorials of Harvey." [London, Churchill, 1875.]

[*Typewritten.*]

Presented by W. W. Keen, M.D., from D'Arcy Power.

Philippe, V. Observations de pratique chirurgicales. [Chartres, 1761–1790.]

Fund for Rare Books.

Shippen, William. Recommendations for an Army medical corps in the Revolutionary war. Photostat copy taken from the original in the library of Congress, by W. O. Owen and presented to E. B. Krumbhaar, M.D. [Washington, 1925.]

Presented by E. B. Krumbhaar, M.D.

*Other Interesting Additions.*

Congressional Medal of Honor awarded to Joseph K. Corson for gallantry in action at Bristoe Station, Va., October 14, 1863, while Assistant Surgeon, 35th Penna. Infantry (6th Penna. Reserve); Congressional Medal of Honor (former design) for which the above was substituted in 1905; Civil War Campaign Badge awarded the above individual, Major Joseph K. Corson; Silver Medal awarded by Congress to Charles B. Hamilton, Surgeon of the U. S. Sloop of War Peacock, in recognition of his services during the action with H. M. S. Epervier, March 29, 1814, and also some papers relative to this medal.

Deposited by Joseph K. Corson's son, Dr. Edward F. Corson, who is also a great-great nephew of Charles B. Hamilton.

Samuel D. Gross, M.D. Gold, diamond-studded medal presented to him by his medical friends at the celebration of his fifty-first year in the profession, April 10, 1879.

Presented by J. Chalmers Da Costa, M.D.

Gold Medal presented to Dr. William Hewson in 1769. The medal always inherited by the oldest medical man in the family.
Deposited by Addinell Hewson, M.D.

A photograph of a Pennsylvania Hospital group including Drs. J. P. Hutchinson, J. H. Gibbon, R. G. LeConte and R. H. Harte.
Presented by George W. Norris, M.D.

A medal struck by the Alumni Association in commemoration of the One Hundredth Anniversary of the Founding of the Jefferson Medical College of Philadelphia.
Presented by Ross V. Patterson, M.D.
at the suggestion of W. W. Keen, M.D.

A photograph of the Tomb of William Withering and a photograph of a field of Digitalis Purpurae grown at Foxglove Farm.
Presented by Mr. F. A. Upsher Smith.

Proof copies of the Portraits of Sir James Mackenzie and Sir Clifford Allbutt.
Presented by Sir Dawson Williams,
through the courtesy of W. W. Keen, M.D.

We have also received during the past year a number of interesting and more or less valuable autograph letters.

Use of the Photostat: During the past year there have been furnished to Fellows of the College 451 prints and to other than Fellows on application, 370 prints. These outside applications include requests from Baltimore; Chicago; Cleveland; Madison, Wisconsin; New York; Philadelphia; Pittsburgh; San Francisco, and Pekin, China.

The work for the Library has been continued as heretofore according to the instructions of the Library Committee; 3971 large and small prints have been made; 11 volumes of incunabula completed as well as various portraits and manuscripts. Up to the present time there have been made photostat copies of 225 incunabula.

There has been an increase to the principal of the Louis A. Duhring Library Fund of $2117.70; to the Morris Longstreth Library Fund of $154.68, and to the Charles A. Oliver Library Fund of $394.02 during the past year. A complete list of all the Funds and the expenditures for the year is given in a previous part of this report. All additional expenses, salaries, binding and various requirements

that may be needed each year have to be governed according to the funds appropriated by the College to the Library Committee annually. The item of binding is most important; the cost has more than doubled, and only the important periodicals and books have been bound. It is understood that an effort is being made to create a Fund, the income to be used for binding, but no official report has been made to the Library Committee.

An account of stock has been taken and any displacements found arranged in their proper order; no report has been made of any books missing from the shelves.

The figures reported showing the number of visitors; number of books consulted, and number of books taken out have no bearing on the increase, resources and capabilities of the Library, but are interesting, perhaps, as indicating, according to the increase in the volumes consulted and the volumes taken out, a greater literary activity in the medical profession of Philadelphia and its vicinity.

That the Library of the College is highly appreciated by those who use it is witnessed by the number of letters which the Librarian receives from time to time stating the satisfaction of the writer for the service it has given him. Many of these letters point out peculiar advantages offered by the Library, directing attention not only to the value of its collections but to the efficient way in which they are handled by those in charge. Our system of classification and method of handling our books is followed by many libraries, whose librarians have sought information concerning it from our Librarian.

Library Committee,

Francis X. Dercum, M.D.,
*Chairman.*

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